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Archives of Neurology and Psychiatry

VOLUME 14 AUGUST, 1925 NUMBER 2

SPONGIOBLASTOMA MULTIFORME

A PRIMARY MALIGNANT FORM OF BRAIN NEOPLASM: ITS CLINICAL AND ANATOMIC FEATURES *

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AND

ISRAEL STRAUSS, M.D.

NEW YORK

Introduction.
Clinical records and anatomic findings.
General consideration of the anatomic findings.
General consideration of the clinical features.
Conclusions.

INTRODUCTION

In July, 1916, under the title of "Spongioblastoma with Unusually Rapid Growth Following Decompression," [1] we published a study of a case which ran an unusual clinical course, and in which we found unusual histologic features. The clinical course was striking because of the acute onset and the rapidity of the development of symptoms which lead rapidly to a fatal termination. In the neoplasm we found the predominant element to be a cell unit similar to the spongioblast, an undifferentiated form of glia cell, and hence we suggested the term "spongioblastoma."

In that report we recalled that it was Virchow [2] who, soon after the discovery of neuroglia, ascribed many brain tumors to glia tissue and named them gliomas. In his original description he characterized these new growths as slow-growing, infiltrating, fairly vascular masses,

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* The work was carried out during the tenure of the Sachs Fellowship in Neuropathology, and was aided by a grant from the Emanuel Libman Endowment Fund.

* Read at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, June, 1924. At the same meeting Cushing and Bailey presented a report of a series to which they also assigned the name spongioblastoma, which appears in this issue. It was apparent to us both that confusion would result from the application of the same name to two groups. Cushing and Bailey have made the suggestion that they adopt the term spongioblastoma indifferentiale for their tumors, and that we use the term spongioblastoma multiforme for ours as descriptive of the wider range of differentiation seen in our series.

1. Strauss, I., and Globus, J. H.: Spongioblastoma With Unusually Rapid Growth Following Decompression, Neurol. Bull. **1**:273, 1918.

2. Virchow, R.: Krankhafte Geschwülste, Vorlesungen **2**:129, 1864.

in which, by virtue of their vascularity, hemorrhages frequently occur, resulting in softening and cyst formation. While these observations still remain as the important distinguishing gross anatomic features of gliomas, his histologic descriptions of such tumors can no longer be considered adequate, in view of our more intimate knowledge of the morphologic and staining properties of glial elements. But, in spite of this better understanding, little advance has been made since Virchow's days in the direction of a better classification of gliomas.

The latter form of neoplasm is now anatomically understood to comprise tumors of ectodermal origin which consist histologically of glia cells and extracellular fibers. They are said to be found only in the central nervous system or its outgrowths, the great majority occurring in the brain. They are described as varying in size from a minute nodule to the size of a complete hemisphere. They are also said usually to be solitary; metastases are of doubtful occurrence, although a few such instances have been reported. Thus Stroebe [3] in one case found a small but well-defined secondary nodule a short distance from the seat of the primary lesion, and considered it as a metastatic focus. Heubner [4] found in the spinal cord a series of independent gliomas extending over an area of fifteen segments. Lensden [5] reported what he considered to be an unusual case of a glioma which spread into the leptomeninges of the spinal cord and brain. This he interpreted as a metastatic form of glioma. Schminke's case [6] is of particular interest to us, since, under the name of glioblastic sarcoma, he records an instance in which the neoplasm formed metastases in the brain and spinal cord. Here it is possible that he was dealing with a neoplasm which falls into the group of the spongioblastomas, which constitutes the subject of this paper.

Gliomas are said to be of slow growth, to extend by infiltration and to form no definite line of demarcation between the normal brain tissue and the neoplastic mass, unless pressure and hemorrhage have led to the formation of a necrotic zone about the periphery of the neoplasm. They are described as composed of cells which tend to differentiate into neuroglia cells, i. e., into cells which form neuroglia fibrils. According to Mallory,[7] if the tumor cells proliferate slowly, neuroglia fibrils will form in large numbers, and these will give rise to the so-called hard

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3. Stroebe, H.: Ueber Entstehung und Bau der Gehirngliome, Beitr. z. path. Anat. u. z. allg. Path. **18**:405, 1895.

4. Heubner: Ueber einen Fall multipler Rueckenmarksgliome mit Hydrocephalus Internus, Arch. f. Psychiat. **34**, 1901.

5. Lensden, P.: Ueber einen eigentümlichen Fall von Gliom des Rückenmarks mit Uebergreifen auf die weichen Häute des Rückenmarks und Gehirns, Beitr. z. path. Anat. u. z. allg. Path. **23**:691, 1898.

6. Schminke, A.: Ein glioblastisches Sarkom des Kleinhirns mit Metastasenbildung in Hirn und Rückenmark, Frankfurter Ztschr. f. Path. **16**:357, 1915.

7. Mallory: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914.

glioma, *the glioma durum;* if, on the other hand, the cells multiply rapidly, few or no fibrils will be produced. This form of tumor is often referred to as the soft glioma, the *glioma molle.* It is in the latter form that diagnostic difficulties are encountered, because of the rich cellular content, the highly proliferative tendency, and the lack of extracellular fibrillae, and also because of certain clinical features which bear such strong resemblance to sarcomas that pathologists have been led to consider them as sarcomatous growths, and to formulate the term gliosarcoma.

Stroebe [8] interpreted the peculiar hyperplastic reaction about blood vessels in such tumors as an expression of mixed tumor formation, since he believed that sarcomatous zones about blood vessels alternated with true gliomatous areas; he named them accordingly: glio-sarcoma.

Borst,[8] on the other hand, realizing the incorrectness of such a name, proposed the term gliosarcomotodes for tumors which clinically bear all the marks of a sarcoma, but which morphologically are allied to the highly cellular gliomas. This, however, has helped little to solve the problem.

This great apparent variation in the cellular make-up and cellular arrangement in these rapidly growing and extremely cellular gliomas has led many into an attempt to classify such tumors. But, unfortunately, little has been accomplished beyond the creation of a large series of new names. Thus we have the "giant cell glioma" [9] characterized by the presence of variable numbers of giant cells; the "adenoglioma," by the alveolar arrangement of the cell elements; the "neuro-epithelioma gliomatosa," by the presence of cystlike structures lined by ependyma-like cells; the "glioma teleangiectaticum," by extreme richness in blood vessels and a tendency to widespread necrotic changes; the "glioma ganglionare," [10] by large cells resembling ganglion cells, and the "myxoglioma" characterized by a gelatinous matrix in the larger part of the tumor growth. Many other purely descriptive terms are used. Kaufman [11] was aware of the misleading character of the term "gliosarcoma" as applied to a tumor of ectodermal origin, since the term sarcoma immediately suggests a mesodermal origin. He introduced the terms "malignant cellular glioma" and "columnar cell glioma" for gliomas rich in the columnar type of cells, particularly when such cells are radially arranged about cystlike structures, hinting, almost apologetically, at the advantage in the use of such a term as "spongioblastoma."

8. Borst: Die Lehre von den Geschwuelsten, 1902.

9. Meyer, O.: Ein besonderer Typus von Riesenzellengliom, Frankfurter Ztschr. f. Path. **14**:185, 1913.

10. Ewing, Jr.: Neoplastic Diseases, a Text-Book on Tumors, Philadelphia, W. B. Saunders Company, 1919.

11. Kaufman: Spezielle pathologische Anatomie, Ed. 6, 1911.

In suggesting these names, he, like many others, responded merely to a desire to find a good descriptive term for some apparent histologic feature characterizing a given tumor, neglecting to utilize the basic histogenetic principles operative in their formation.

We were guided in the study of our first case by the belief that neuro-ectodermal tumors are subject to the same laws or forces which determine the histogenetic features of tumors derived from other sources, other tissues or other germ layers; and we believe that we found anatomic basis to support the idea that glioblastic tumors can produce various forms, each corresponding to a given phase in the process of differentiation of the glioblasts.

Indeed, it appeared to us then that there is a definite and rather striking parallelism in the way in which the kind of tumor we described and malignant neuroblastomas, acquire their histologic characters. What is still more suggestive is the fact that in the case of the so-called malignant neuroblastoma a form of neoplasm now definitely traced to the primitive neuroblasts, almost identical difficulties had to be met and equally numerous errors were made before their true derivation and true character were established. They also have been grouped for a long time with the sarcomas, and only through the contributions of Marchand,[12] Wiesel,[13] Wright,[14] Landau,[15] Martius,[16] Symmers,[17] Wohl,[18] Glosmet,[19] Harbitz,[20] Lambert [21] and others have they been

12. Marchand, F.: Ueber eine Eigentümliche Erkrankung des Sympathicus, der Nebennieren und der peripherischen Nerven—ohne Bronzehaut, Virchows Arch. f. Path. Anat. **81**:477, 1880; Beiträge zur Kenntnis der normalen und pathologischen Anatomie der Glandula Carcotica und der Nebennieren, Festschrift, Rudolf Virchow, Internat. Beitr. z. wissensch. Med. **1**:535, 1891.

13. Wiesel, J.: Bemerkungen zu der Arbeit H. Kuesters über Gliome der Nebennieren, Virchows Arch. f. path. Anat. **180**:553, 1905.

14. Wright, J. H.: Neuocytoma or Neuroblastoma a Kind of Tumor Not Generally Recognized, J. Exper. Med. **12**:557, 1910.

15. Landau, M.: Die malignen Neuroblastoma des Sympathikus, Frankfurter Ztschr. f. Pathol. **11**:26, 1912.

16. Martius: Maligner Sympathoblastentumor des Halssympathikus teilweise ausdifferenziert zu gutartigem Ganglioneurom, Frankfurter Ztschr. f. Pathol. **12**:442, 1913.

17. Symmers, D.: A Recurrent Neuroblastoma of the Scapular Region, J. A. M. A. **60**:337, 1913.

18. Wohl, H. R.: Neuroblastomata. With a Study of a Case Illustrating the Three Types That Arise from the Sympathetic System, J. Med. Res. n. s. **25**: 205, 1914.

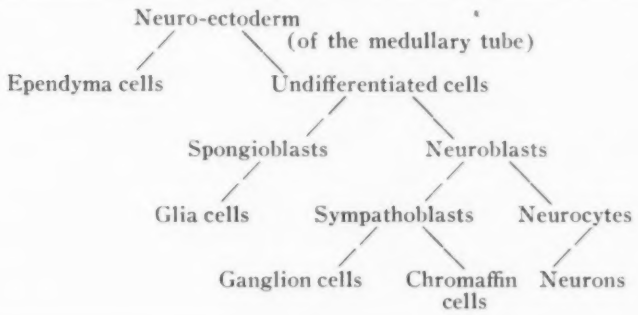
19. Glosmet, D. J.: Malignant Sympathicus Tumor of the Right Suprarenal, Arch. Int. Med. **15**:341 (March) 1915.

20. Harbitz, F.: Tumors of the Sympathetic Nervous System and the Medulla of the Adrenal Glands, Especially Neuroblastoma, Arch. Int. Med. **16**:312, 1915.

21. Lambert, R.: Malignant Neuroblastoma, Proc. N. Y. Pathol. Soc., n. s. **17**: 1917.

rescued from this "melting pot" of malignant tumors and have been assigned their rightful place. Through the efforts of Kuester,[22] Alezais and Peyron,[23] Schilder,[24] Pick,[25] Pick and Bielschowsky,[26] Herxheimer,[27] Dunn,[28] Thomas,[29] Homma [30] and many others, we have learned to recognize several other related forms of tumor of neuro-ectodermal derivation, such as, the sympathoblastoma, ganglioneuroma, malignant glioma of the sympathetic and paranganglioma or phaochromatocytoma. Each of these tumors is identified by the predominance of a form of cell which represents a given stage in the differentiation of the parent neuroblast into the mature neuron, and thus can be traced to the corresponding, incompletely specialized cell unit, such as sympathoblast, ganglioblast or chromaffin cell (Tables 1 and 2).

TABLE 1.—*Stages in Differentiation of Various Components of Primitive Neuro-Ectoderm Into Mature Cellular Units of Central Nervous System and Its Derivatives*



22. Kuester, H.: Ueber Gliome der Nebennieren, Virchows Arch. f. path. Anat. **180**:117, 1905.

23. Alezais and Peyron: Un groupe nouveau de tumeurs epethéliales; les paraganglions, Compt. rend. Soc. de biol. **65**:745, 1908.

24. Schilder, Paul: Ueber das maligne Gliom des sympathischen Nervensystems, Frankfurter Ztschr. f. Pathol. **3**:317, 1909.

25. Pick, L.: Berl. klin. Wchnschr. **49**:16, 1912.

26. Pick and Bielschowsky: Ueber das System der Neurome und Beobachtungen an einem Ganglioneurom des Gehirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:391, 1911.

27. Herxheimer, G.: Ueber Tumoren des Nebennierenmarkes, inbesondere das Neuroblastoma sympathicum, Zieglers Beitr. z. pathol. Anat. **57**:113, 1914.

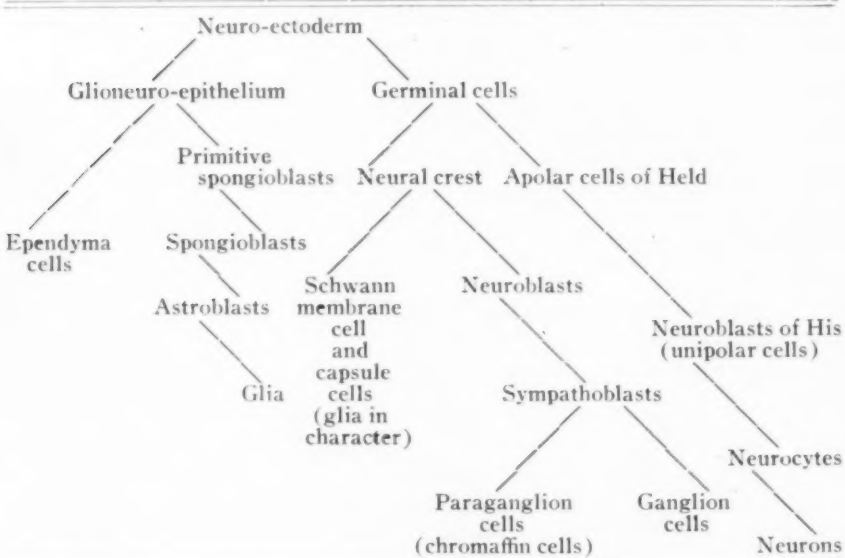
28. Dunn, J. S.: Neuroblastoma and Ganglio-Neuroma of the Suprarenal Body, J. Pathol. & Bacteriol. **19**:456, 1914-1915.

29. Thomas, E.: Ein chromaffiner Tumor der Nebenniere, ein weiterer Beitrag zu den Markgeschwülsten der Nebennieren, Frankfurter Ztschr. f. Pathol. **16**:377, 1915.

30. Homma, H.: Ueber einen Fall von Ganglioneuroma Sympathicum der Region retromandibularis, Zieglers Beitr. z. pathol. Anat. **72**:323, 1924.

Gliomas, no matter what their histologic features may be, constitute an important and large division among the true neuromas, and therefore are not only to be considered as neuro-ectodermal in derivation, but ultimately must be traced to that division of the primitive neuro-ectoderm which is destined to develop into the glial components of the central nervous system. It is also true that this division of the primitive neuro-ectoderm, similar to the neuroblastic division, undergoes many changes before the final, fully differentiated end-product—the glia cell—is reached. It is therefore apparent that in the course of differentiation many transitional stages will be encountered. These stages in the differentiation of various components of the primitive neuro-

TABLE 2.—*Modification of Table 1*



ectoderm into the mature cellular units of the central nervous system and its derivatives are represented graphically in the following diagram, which we borrow from our first report.

In order to meet some of the more recent views, particularly those of the school of Cajal, Table 1 demands a few modifications; nevertheless, it still remains as a good working schema showing the various stages the primitive neuro-epithelium is passing through in the process of complete differentiation into the highly specialized nerve units. The main difference between Table 1 and Table 2 is to be found in the addition of several transitional stages and in the change of the level at which the ependyma cells are given off.

The differences between Tables 1 and 2 are not such as to affect the views we previously expressed, and do not require any essential modifi-

cation of those views. In both of these tables, early in the histogenetic process there is a split into two main divisions: the spongioblasts and the neuroblasts. The spongioblasts are the parent cells of the glia, while the neuroblasts develop into the various neuron forms of the cerebrospinal axis and its derivatives, including the migrating sympathoblasts. Certain of these sympathoblasts are set aside for the acquisition of a new character—that of a cell of internal secretion—and form the so-called chromaffin cells, the constituent elements of the chromaffin bodies. Such a group of cells is split off from the celiac ganglion, soon to be engulfed by the mesodermal component of the suprarenals and to form the medulla of that structure.

A study of Table 2 shows that a sound classification for a large variety of neoplasms which take their origin from the neuroblastic branch of the differentiating neuro-ectoderm has been secured by establishing the morphologic relationship of each variety of tumor to a formative cell of a corresponding stage in the development of the specific nerve elements. But thus far little attempt has been made to group the glioblastic forms of tumor on similar lines, though it is patent that the same histogenetic factors are operative in the development of gliomas as in the development of the neuroblastic tumors. There can be no doubt that just as the neuroblast, a transitional type of neuron-forming cell, is responsible for the development of neuroblastomas, so the spongioblast, a transitional, unripe form of glia cell, may form the basis for the development of a tumor which can rightly be designated as spongioblastoma. Both types of formative cell, the neuroblast and spongioblast, represent an almost similar level of differentiation in their respective divisions of the primitive neuro-ectoderm, and should develop into tumors which possess many features common to both. They are both—neuroblastomas and spongioblastomas—richly cellular, very proliferative and rapidly growing. The first is capable of metastasis, the latter of multiplicity of growth centers. Histologically, while there are striking differences in the type and size of their cells, they both show roset formation and clustering of cell groups.

The similarity in the morphology of these two genetically related tumors is so marked that it led Ribbert into the error of considering a tumor of the suprarenal, described by Küster, as a malignant glioma; later, however, this was identified by Wiesel [13] as a neuroblastoma. This is recalled by Ribbert [31] in his extremely important work on spongioblastoma. In this work, which appeared two months after the publication of our first paper on spongioblastoma,[1] Ribbert presents a group of tumors which, in spite of certain variations in their morphologic appearances, he assembles under the name of spongioblastoma,

31. Ribbert, H.: Ueber das Spongioblastom und das Gliom, Virchows Arch. f. path. Anat. **225**:195, 1918.

because they show several common features which stamp them as neoplasms derived from the undifferentiated glia elements—spongioblasts. It is his opinion also that gliosarcomas have no existence. He argues on grounds similar to those we have advanced that the term gliosarcoma presupposes that two germ layers are engaged in the development of such a tumor. Were tumors, not teratomatous in character, he says to be derived from two germ layers, we should expect to find in a great majority of instances a great cellular assortment ("Vielgestaltigkeit") and variability in the histologic make-up in a given tumor, and in but few instances should we find tumors limited to one type of tissue and its direct derivatives.

He regards the presence of ependymal, cystlike structures and roset formation as indication of the embryonal character of the tumors, and objects to the frequently expressed view that mature glia cells may revert to type so as to give rise to embryonal structures.

In reviewing Ribbert's article we were struck by the close similarity between his drawings and the numerous photomicrographs which we had made from our material. The clinical histories of cases due to a tumor of this class present features which are likewise important in differentiating this type of growth from the other forms of glioblastic tumors, and add additional support to their morphologic differentiation.

REPORT OF CASES

Case 1.—*History.*—G. W., admitted to the Montefiore Hospital on Aug. 4, 1917, had always enjoyed good health, except for severe constipation with accompanying headaches which were accentuated during the menstrual periods She frequently vomited during her headaches. She had never suffered from any acute infectious disease. Three weeks before admission to the hospital, while bathing in the surf, she was thrown several times by the breakers, and on one occasion struck her head. Following this, she suffered from frontal headache, but no more severe than previously. There was no hemorrhage from the nose, ears or mouth or any disturbances in motor power, speech or mentality. About five days later, she suddenly developed weakness in the left arm and leg, and this became gradually intensified. There was no fever. Acute poliomyelitis was suggested, but the error of this diagnosis was soon discovered as projectile vomiting developed, the headaches became more severe and localized to the frontal region, and the upper and lower extremities became weaker and spastic. With this there was a tendency to lapse into stupor, from which, however, she could be easily aroused.

Examination.—On admission to the hospital, she appeared dull, listless and somnolent. Her replies to questions were slow and monosyllabic. She complained of considerable pain in the back of the neck, and there was slight rigidity. The olfactory sense was intact, vision was unimpaired, but bilateral optic neuritis of equal intensity on both sides had developed. The pupils were unequal, the right was greater than the left; both reacted well to light and in accommodation. There was left facial weakness, involving the lower two thirds of the face and the left upper and lower extremities presented at first spastic paralysis, but later became flaccid. There was generalized hyperflexia, more

active on the left than on the right; exhaustible ankle clonus on the left and a Babinski sign on the left. There was loss of tactile and deep sensibility in the left arm and leg and a stereognosis in the left hand. Pain sense apparently was more acute on the left side.

The cerebrospinal fluid was under normal pressure, showed a normal cell count and a moderate increase of globulin. The Wassermann test on both blood and cerebrospinal fluid was negative.

The diagnosis of a subcortical fronto-parietal neoplasm was made.

Three days after admission, the patient became semicomatose, the choking of disk progressed rapidly, and spastic hemiplegia became complete.

Operation and Course.—The same day a right cerebral decompression was performed by the removal of a large bony flap. On opening the dura, the brain

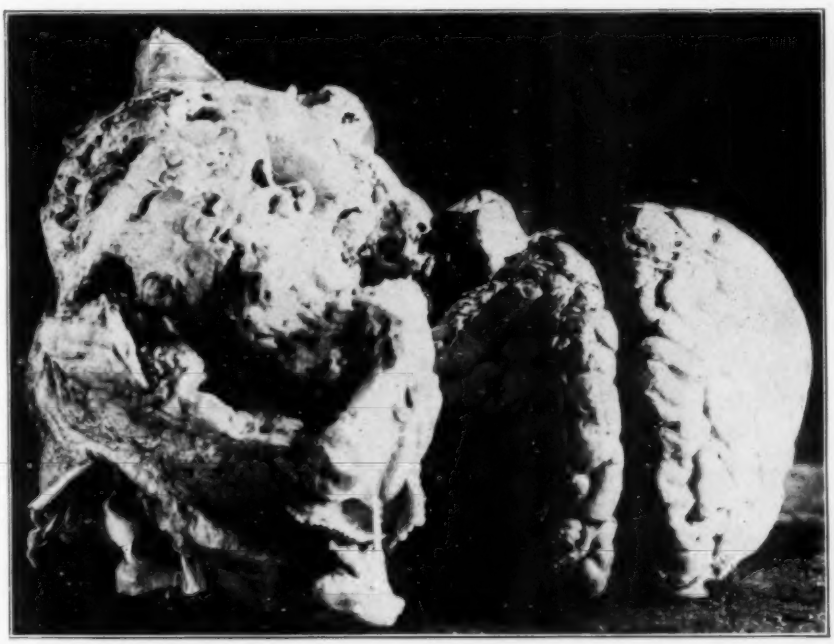


Fig. 1 (Case 1).—Enormous size attained by the cerebral neoplasm, in a relatively short time.

was found to be under marked pressure. Aspiration in the direction of the ventricles was made, and a few fragments of brain tissue were removed for histologic study. Following the decompression there was no change in the physical signs except for considerable reduction in papilledema.

The subsequent course of the disease was rapid. Contractures developed rapidly in the left upper and lower extremities. A hernia cerebri developed and grew rapidly until it became tremendous, and somewhat later the skin over it began to slough. The general condition declined rapidly, and the patient died three months after admission to the hospital.

Gross Anatomy.—The brain was of approximately normal size, the left hemisphere presenting nothing of significance except flattening of the convolutions. The right hemisphere on the other hand presented a striking picture

(Fig. 1). A large mass, 17 cm. long, 14 cm. wide and about 10 cm. deep was attached by a broad peduncle to the substance of the right cerebral hemisphere replacing its dorsolateral surface over an area covering the greater part of the frontal, parietal and temporal lobes. The peduncle consisted of a mass of soft but friable hemorrhagic and extremely necrotic tissue. On moving it aside, there was a large cavity communicating with the lateral ventricle. The main mass supported by the peduncle was surrounded by a thin capsule of soft white tissue beneath which the necrotic and vascular neoplastic substance was seen.

Microscopic Anatomy.—The dominant type of cell was pyriform, with a vesicular nucleus, and filled with deeply staining granules. These cells were not unlike those which are so characteristic of neuroblastoma (Fig. 2). Many of these cells gave off blunt processes, some of which come in contact with contiguous cells, giving rise to a reticulum. Round cells with variable amounts of

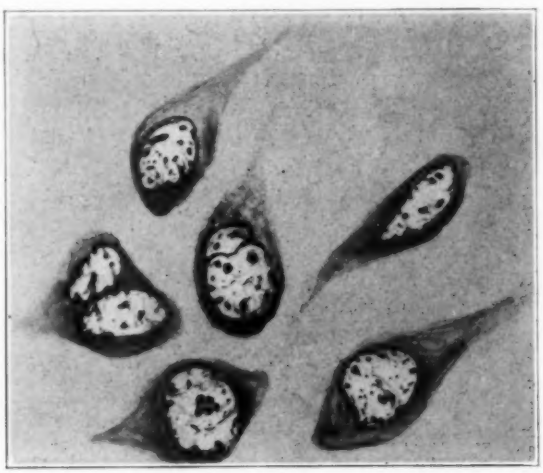


Fig. 2 (Case 1).—Camera lucida drawing of predominant type of tumor cell, pyriform and giving off short blunt processes. They contain one or two nuclei, which are clear and contain deeply staining chromatic granules (Zeiss ocular 6 ×; objective, 16 mm.).

cytoplasm were also found in large numbers. They were supported by a fairly homogeneous matrix, which in places presented a granular or reticular appearance and assumed the character of a syncytium. Cells irregular in outline, with a thick process at one pole of the cell and with a rounded base were particularly interesting because of their relationship to blood vessels or cystlike structures. They grouped themselves about such structures in a radiating fashion, with their processes running in more or less parallel lines and at right angles to the enclosed cyst or vessel walls in such a way as to take on an actiniform appearance (Fig. 3).

Giant cells were numerous and conspicuous, and were diffusely scattered throughout the growth. They varied in size, outline and nuclear contents. Some were relatively small and contained but one deeply staining nucleus, while the great majority were large and often contained as many as six to eight well formed and well defined nuclei. In some the nuclei gathered at one pole; in others they were distributed at both. In still others, mature, independent

nuclei were arranged in the form of a ring at the periphery of the cell. Many of these cells had their nuclei in the center of the cell, where they were so grouped as to overlap each other. This variation in the distribution of nuclear material can be regarded as the expression of atypical (amitotic?) cell division. The cytoplasm of the giant cells was variable in amount and assumed various forms: round, oval, stellate or flask-shaped, with an occasional blunt process given off at the narrowed pole of the cells (Fig. 4). Extracellular glia fibers were seen only in a few small isolated patches.

The outstanding histologic features of this tumor are the large number of the undifferentiated, neuro-epithelial cells, the presence of spongioblasts with marked proliferative tendencies and the alveolar, roset and cystlike formations (Fig. 5).

Case 2.—*History.*—E. R., aged 10, admitted to the hospital April 12, 1921, for four weeks previous to admission had complained of occipital headaches and attacks of dizziness, and two weeks previously had fallen on her forehead and had been dazed but not unconscious. From the time of the fall, the patient began to complain of diplopia, which persisted. She felt weak, went to bed and was unable to walk on account of weakness. She felt drowsy and at times restless. There was an occasional twitching of the right leg.

Examination.—The patient was in bed, with her head turned to the right and her eyes to the left. She complained of diplopia and stated that when she sat up objects seemed to move from left to right. Her mentality was clear and her memory was good. A slight turning of the head produced violent vertigo. She had a right hemiparesis with ipsolateral hypotonia, ataxia, increased deep reflexes and a bilateral Babinski sign. The tongue and jaw deviated to the right. There was supranuclear involvement of the facial nerve. A right adiadokokinesis was present. The pupils were unequal, the left being more active than the right; both reacted promptly to light and in accommodation; there was nystagmus in all directions on movement, most marked to the right; there was weakness of the right external rectus and of the right superior rectus, and bilateral corneal hypesthesia. The abdominal reflexes were absent, and there was atrophy of the left half of the tongue.

Course.—April 14: The optic disk showed slight blurring of the nasal borders.

April 16, the otologist reported that hearing was normal. The diagnosis rested betwen encephalitis and cerebellar neoplasm. May 2, right hemiparesis and the right Babinski sign were more marked, and the Babinski sign was also present on the left; speech was thick and bulbar; the mental state was duller, and there was tremor of the head. The head was tilted to the right, and there was bilateral papilledema.

May 11: Hemiplegia was almost complete on the right side. The head was in right cerebellar tilt. There was some dysphagia and regurgitation of fluid. Papilledema was increased.

May 14: The patient's condition rapidly declined, and she died that evening.

Gross Anatomy.—The dura presented no abnormal features. The pia-arachnoid presented no adhesions or infiltration. At the base of the brain, it was deficient in some areas because of tumor involvement.

The cerebral hemisphere showed no abnormalities except marked flattening of the gyri.

At the base of the brain, the normal topographic land marks were to a great extent obliterated by a diffusely spreading mass which apparently extends from the left cerebellar angle over the pons to the corresponding

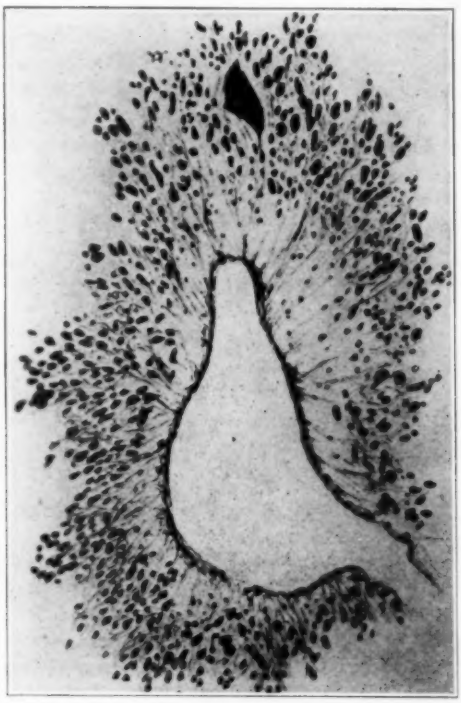


Fig. 3 (Case 1).—Camera lucida drawing showing the ependymal cystlike structure. (Zeiss ocular, 6 ×; objective, 16 mm.)

Fig. 4 (Case 1).—Camera lucida drawing showing various types of giant cells. (Zeiss ocular, 6×; objective, 16 mm.)

angle on the opposite side, then downward covering the medulla and upward covering the left cerebral peduncle. A portion of the brain stem, represented by the medulla, pons and midbrain, was infiltrated by this diffusely growing mass. The acustic nerve on the left side was extremely soft and mushy. The third and fourth nerves on the left side were thin and ribbon-like. The fifth was caught in the mass and could not be readily isolated. The sixth were both extremely thin. The roots of the twelfth were covered by the neoplastic mass. Only a few fine rootlets could be found.

Microscopic Anatomy.—Sections of the tumor mass showed the latter to be composed of numerous flask-shaped and stellate cells. Numerous giant cells and roset formations were seen in the microscopic field. The histologic features bore a strong resemblance to those seen in Case 1, and need not be described.

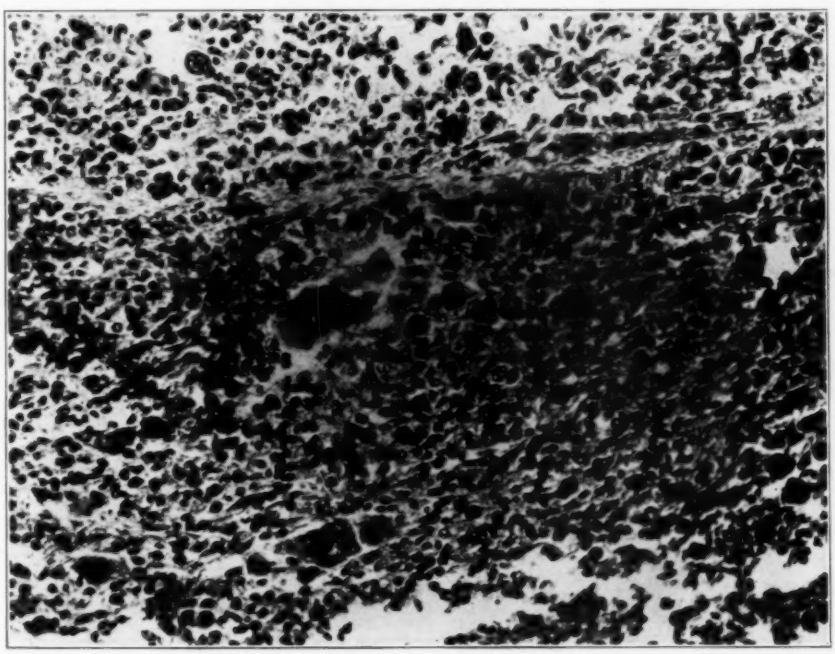


Fig. 5 (Case 1).—General histologic appearance of the tumor.

CASE 3.—*History.*—F. K., aged 51, admitted to the hospital, July 5, 1922, three weeks before admission suffered from what was diagnosed as acute polyarticular rheumatism. She apparently recovered. Two weeks before admission, while sitting in bed, she suddenly became dizzy, fell and broke her nose. She made a good recovery but one week later, seven days before admission, while up and about she suddenly developed an intense headache, most pronounced in the right frontal region. The headache was violent and throbbing and was associated with slight drownsiness. With the headache, which persisted, on the following day there developed weakness of the left side of the face and slight weakness of the left arm. The drowsiness became more pronounced and continued for twenty-four hours, when signs of meningeal involvement, bilateral Kernig sign and rigidity of the neck were noticed. With this there developed

inequality of the pupils—the right was greater than the left. Bilateral Babinski signs also appeared. At this time a diagnosis of encephalitis was suggested. Vomiting occurred on the day before the meningeal symptoms developed. There was no elevation of temperature. The condition became progressively worse, and complete left hemiplegia developed. The patient went rapidly into a stupor. At this time a lumbar puncture was performed. The findings were negative. Death occurred on the day of admission.

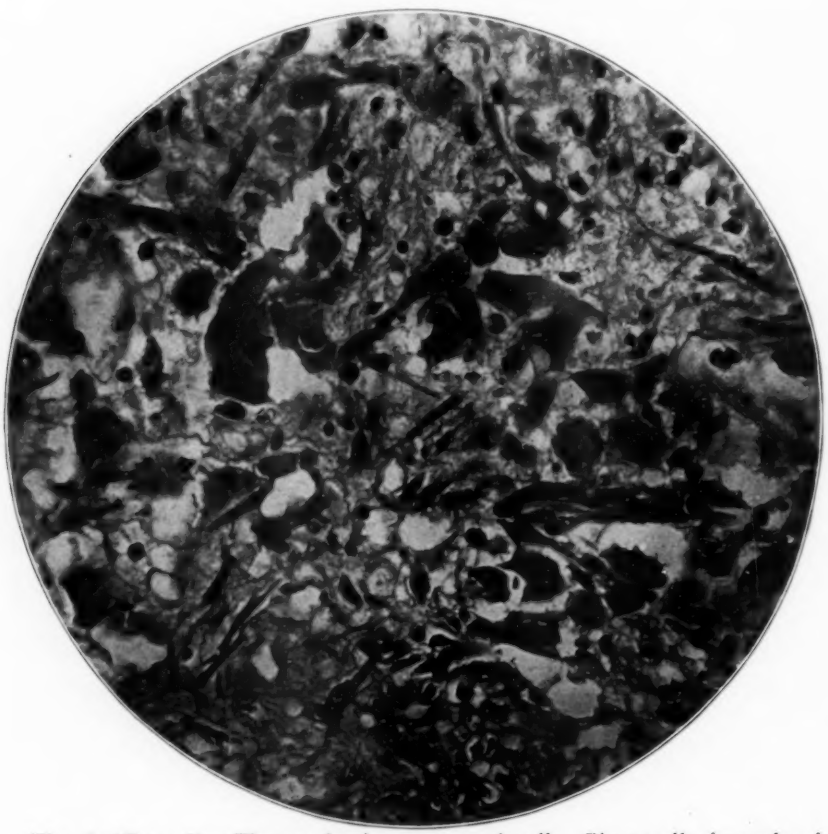


Fig. 6 (Case 3).—The predominant type of cell. Giant cells irregular in outline, containing one or more deeply staining nuclei and a few fusiform and flask-shaped cells are seen in the field.

Gross Anatomy.—The dura and pia-arachnoid show no abnormality. The brain appeared somewhat shrunken and flattened. The vessels were markedly thickened. The right temporal lobe was soft and fluctuating and on incision was found to be replaced by a large, soft, brownish-red neoplastic mass. Recent hemorrhages were seen in the mass. The lateral ventricles and the basal ganglia were deflected to the left by the tumor.

Microscopic Anatomy.—The tumor presented a fairly uniform histologic picture. The dominating type of cell was large, irregular in shape, containing one or more nuclei and in some instances gave off blunt processes (Fig. 6).

Fusiform and flask-like cells were also found in large numbers. The arrangement was not unlike that described in Case 1. This tumor, like that in Case 1, was marked by extensive areas of necrosis, numerous hemorrhagic foci and great vascularity.

CASE 4.—*History.*—G. L., aged 52, admitted to the hospital, June 6, 1923, had had a nasal operation twelve years before. No other facts of importance were recorded except that hearing became impaired following trauma during childhood. About three weeks prior to admission the patient complained of severe frontal headaches, particularly over the right eye. The pain soon extended to the right shoulder and arm. There was no vomiting, no loss of motor power and no loss of sphincter control.

Examination.—The patient was mentally retarded; she did not seem to grasp questions easily; she showed a somewhat childish emotional state; she was plaintive; her sense of smell apparently was normal. The pupils were unequal, the right was greater than the left and both reacted poorly in accommodation. There were ptosis of the left eyelid and slight left facial weakness. The tongue deviated to the left. The deep reflexes were equally exaggerated; and the abdominal reflexes were equally diminished. There were right Babinski, Gordon and Oppenheim signs. Gait and station apparently were normal. The sensory examination was unreliable. Fine coordination tests were poorly carried out.

Course.—On June 7, the patient showed marked engorgement of veins in both fundi with marginal blurring of the right disk. There was also tenderness in the right temporal region. On June 8, the pupils did not react to light; there was bilateral ptosis, rigidity of the neck and Kernig's sign, and the patient was drowsy but could easily be aroused. Diagnosis rested between "encephalitis" and "brain neoplasm." Lumbar puncture showed that the fluid was clear and contained eight cells. The patient died on June 9.

Gross Anatomy.—The dura was tense and bulging. The pia everywhere was smooth and glistening. There was a moderate degree of congestion in the smaller pial vessels over the entire dorsolateral surface of the cerebral cortex. There was a moderate degree of congestion in the region of the midbrain and in the interpeduncular space. The gyri of the cerebral hemispheres presented a marked degree of flattening. The cranial nerves, midbrain, pons and medulla presented no gross abnormality.

On incision, the right cerebral hemisphere presented a neoplastic mass in the right frontoparietal region. The mass measured about 4 by 5 cm. and was surrounded by a wide zone of edema; another independent mass was found more anteriorly on the right side of the corpus callosum. In the midbrain marked congestion with areas of softening were noted (Fig. 7).

Microscopic Anatomy.—Section through the center of the tumor presented a most unusual cellular picture. The most conspicuous type of cell was a large mononuclear cell (Fig. 8), irregular in outline, occasionally giving off a long process directed to the wall of a blood vessel (Fig. 9). Giant cells with their nuclei, two to six in number, arranged most commonly at the periphery of the cell, were also found frequently.

CASE 5.—*History.*—G. F., aged 23, admitted to the hospital, May 31, 1924, four months previous to admission had had difficulty in raising the right arm and in lifting weights with it. Limitation of motion in the right upper extremity followed. At the Vanderbilt Clinic, twitchings of the muscles and anesthesia of the right shoulder were observed. Ten days before admission

Fig. 7 (Case 4).—Two independent tumor masses representing independent centers of growth.

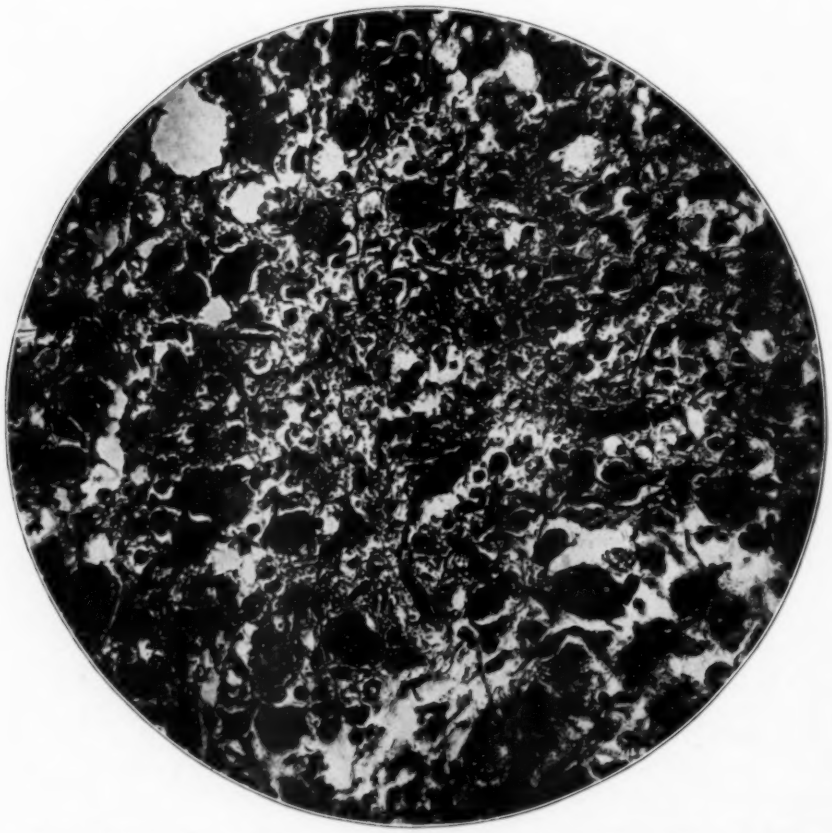


Fig. 8 (Case 4).—Characteristic mononuclear giant cells which bear strong resemblance to monster glia cells.

his neck became stiff and tender; there was a dull pain in the back and sides of his neck, which extended upward to the right postauricular area. (Following a hyperpnea test, persistence of twitching in the right side of the face was noticed.)

Examination.—The patient held his head and neck inclined to the left. There was a suggestion of left external rectus weakness as the patient saw double in looking to the extreme left. The fundi were negative. There was

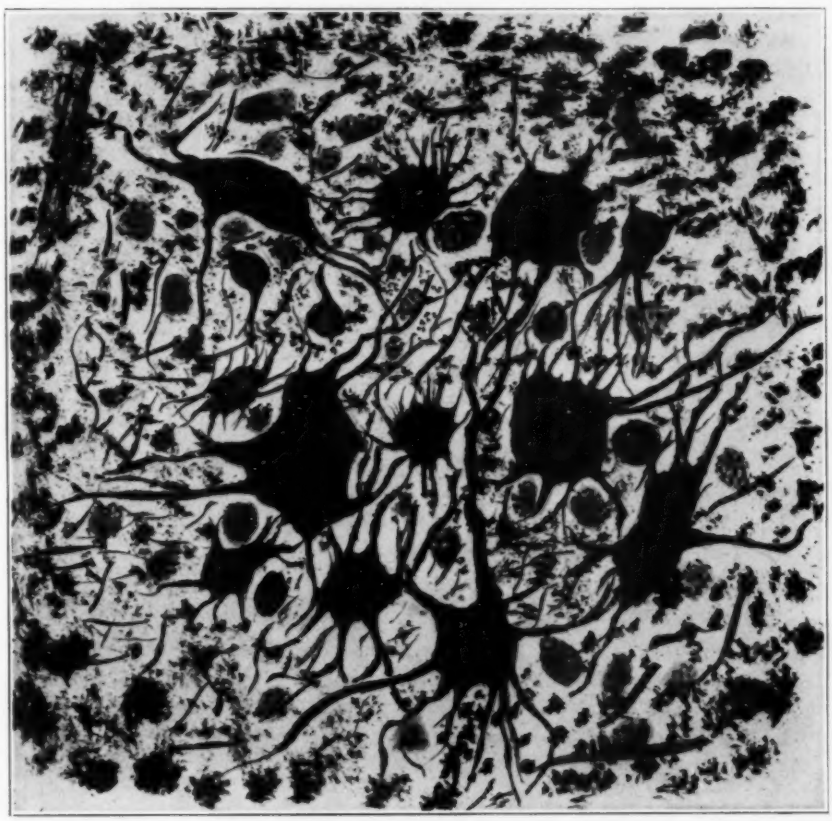


Fig. 9 (Case 4).—Camera lucida drawing showing the morphology of the glia monster cells. Their long processes are well brought out by the specific glia stain and are seen in places to be directed to a blood vessel. (Gold sublimate method; Zeiss ocular, 6×; objective, 16 mm.)

spasticity of the right arm and forearm, including the fingers. The left side was normal. The reflexes on the right side could not be obtained on account of spasticity; the left were active. The knee reflexes were increased on the right; there was a tendency to patellar clonus and a Babinski sign on the right. There was marked diminution of pain sense in the distribution of the fourth cervical nerve on the right side and slight diminution from the third cervical to the fifth sacral on the left side. The Queckenstedt test was negative. Subsequently thermal discriminative sense was lost from the the first lumbar to

the fifth sacral on the left, and there was marked decrease in the fields of the fourth, fifth and sixth cervical nerves.

Operation.—On June 1, an exploratory laminectomy in the cervical region was performed. There was no evidence of tumor. One and a half hours after operation the patient became cyanotic and died.

Gross Anatomy.—On opening the dura and exposing the cord, a fusiform swelling was noted. This swelling was somewhat more marked on the right

Fig. 10 (Case 5).—Sections of the spinal cord showing the extent and high vascularity of the neoplasm.

side, with its greatest diameter at the level of about the fifth cervical segment. At this point the right side of the cord showed bluish discoloration (Fig. 10). The swelling, which was somewhat doughy, extended almost through the entire length of the portion of spinal cord removed (from the second cervical to the fourth dorsal). Its lower level was about the third dorsal segment. At the level of the fourth dorsal segment another small protuberance was noted on the left side of the cord, measuring about 7 mm. in diameter. On incision

through the main fusiform mass the normal markings of the cord were obliterated, and there was a large hemorrhagic mass which occupied almost two thirds of the cord. The extreme left side of the cord retained its white appearance, but definite separation into gray and white matter was not visible. On tracing the hemorrhagic mass upward and downward, it was found to diminish rapidly in size, and to be replaced by grayish-white neoplastic tissue. The smaller mass below was not hemorrhagic, was of firm consistency, and fused with the structure of the cord.

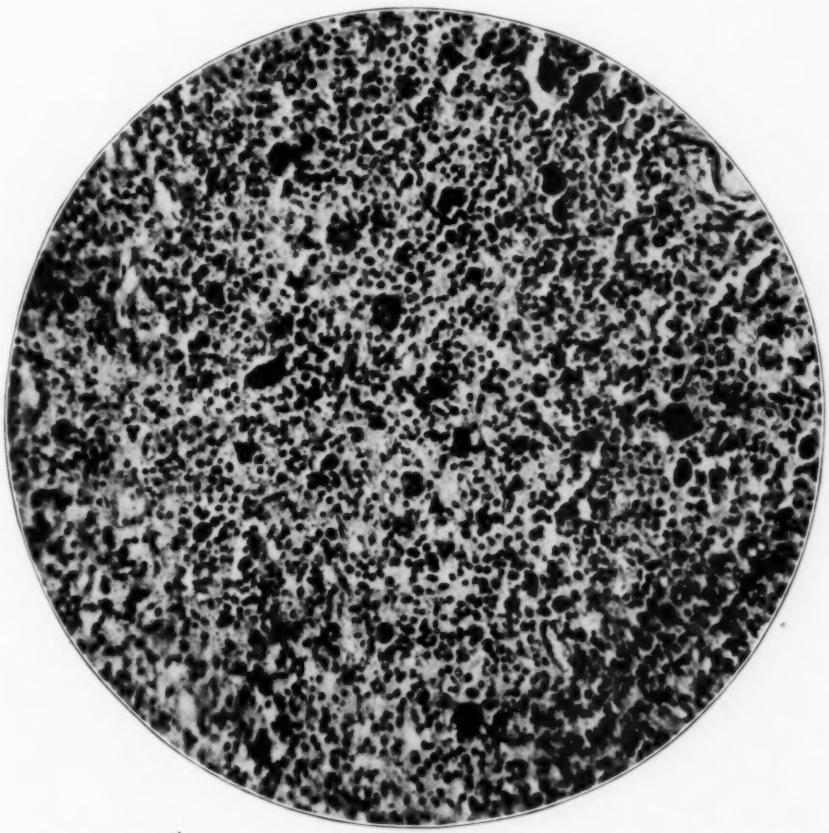


Fig. 11 (Case 5).—Low power appearance of a typical field of the tumor.

Microscopic Anatomy.—Sections through the main tumor mass presented a histologic picture of a highly cellular, infiltrative, malignant form of glioma (spongioblastoma). Here again giant-like cells with numerous nuclei and roset formation were seen in large numbers (Fig. 11).

Case 6.—*History.*—M. S., aged 52, admitted to the hospital, March 10, 1924, had had hypertension for some time, with occasional nosebleed and headache. One week before admission, the patient noticed that she could not pick up articles with ease with her right hand. This was followed by flattening of the face, accompanied by some difficulty of speech. At times she was unable to find certain words. She also noticed that her memory was somewhat

impaired. The weakness of the right arm became more marked and spread to the right lower extremity.

Examination.—On admission, she appeared somewhat older than the given age. She was poorly developed, poorly nourished, and there was puffiness of the face, especially under the eyelids. Her general physical condition presented no striking findings except evidence of general arteriosclerosis and hypertension. The blood pressure was: systolic, 188; diastolic, 85.

Neurologic examination revealed that the patient was apathetic, somewhat resistant and confused, with some impairment of orientation. She was emotionally unstable. Speech was impaired, and she stumbled over words and presented a picture of a mild form of so-called motor aphasia. The pupils were slightly unequal, the right being larger than the left, and they reacted well to light but not in accommodation. There was no impairment of ocular movements, no nystagmus and no impairment of vision. The fundi, with the exception of slight haziness of the disk margins and slight engorgement of the veins, apparently were negative. There was weakness in the field of the right facial nerve involving its lower two-thirds. The palate on the left side lagged behind the right. The tongue deviated to the right. There was weakness of the right upper and lower extremities, with some spasticity. The deep reflexes were hyperactive, more markedly on the right side than on the left. The abdominal reflexes were not elicited. There was a definite Babinski sign on the right, but no clonus. Examination of the fundi showed the arteries smaller than normal and tortuous; the veins were widened, more markedly on the left. Lumbar puncture was negative. Urinalysis showed a few casts and a few white blood corpuscles. The Wassermann test was negative.

At this time the diagnosis of cerebral arteriosclerosis, with localized softening of the left motor area, was considered to be the most plausible, because of the acute onset, rapid progression, evidence of general arteriosclerosis, absence of papilledema and the emotional instability, and at first tumor was excluded on similar grounds. Cerebral syphilis was ruled out by the negative serologic findings. The first days of the patient's residence in the hospital were marked by fluctuations in the mental state, and by slight progression in the paretic features. Careful examination of the eyegrounds, however, disclosed slow progressive swelling on the optic disk. Three weeks after admission, the slightly blurred margins of the disks gave place to definite swelling, but this condition was still considered by the ophthalmologist as a form of neuroretinitis of arteriosclerotic origin. A few days later retinal hemorrhages began to appear on and around the disks, and the swelling increased from 2½ to 3 diopters; the hemorrhages in the next few days became numerous on the right side. On April 2, the swelling of the disk measured 5 diopters.

Course.—A ventrilography was then advised and carried out and led to the following conclusions: No air entered the lateral ventricle from the right. It was suggested that there was a deep tumor on the left side in the temporal lobe pressing on the left foramen of Monro. In view of this finding, craniotomy was performed, with partial excision of the tumor in the left cerebral hemisphere.

Following operation, the patient's condition declined rapidly, with death occurring forty-eight hours after operation.

Gross Anatomy.—The brain was under increased intracranial pressure. The gyri were flattened, particularly over the left frontoparietal lobe, where there was a crater-like excavation, the bottom of which was filled with dark brown, friable, necrotic material in the substance of which were seen several small

pearly white nodules (Fig. 12). On section, this tumor mass and the surrounding necrotic zone was seen to extend from within 2 cm. of the frontal pole backward throughout the frontal and parietal lobes as far as the beginning of the occipital lobe. The tumor was conical in outline, the apex of which was directed forward. The tumor mass was highly vascular, hemorrhagic, fairly well circumscribed and demarcated from the surrounding highly edematous zone. In the latter area a few other small neoplastic masses were noted which apparently formed independent growth centers.

Microscopic Anatomy.—The histologic picture was strikingly similar to that in Case 3. Here again were numerous giant cells with grotesque nuclear arrangement and fragmentation; structures like ependymal cyst and "roset"

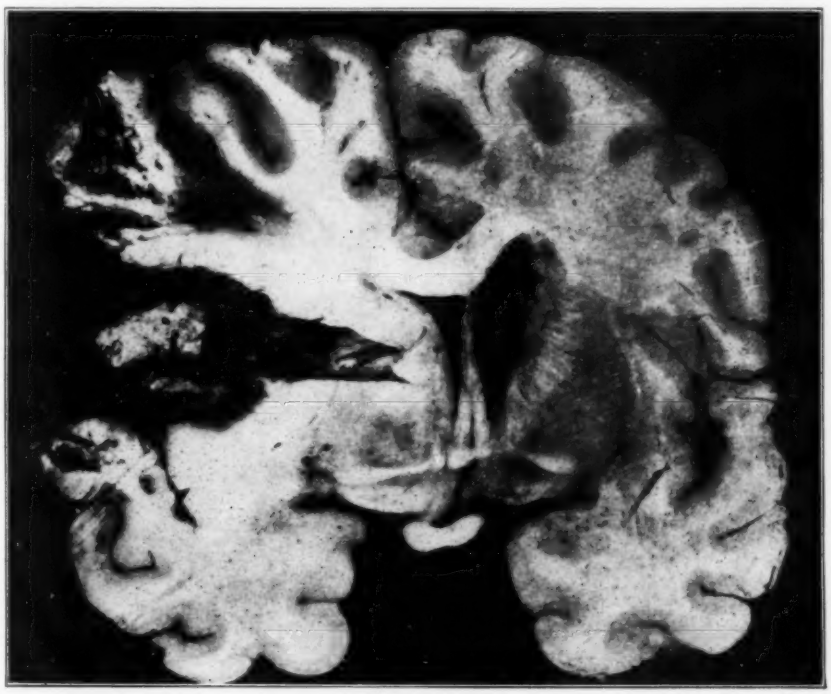


Fig. 12 (Case 6).—Appearance and location of the tumor in Case 6.

formations were well represented (Fig. 13). The necrosis and vascularity were outstanding features in this tumor.

Case 7.—*History.*—A. S., aged 63, admitted to the hospital, May 12, 1924, one year before had an attack of rheumatism and bronchitis, and evidence of hypertension, with a trace of albumin in the urine. Two months before admission it was noticed that the patient was somewhat dazed and not interested in what was told to her. She became somewhat uncommunicative and would speak very little but speech was coherent and well articulated. She complained of frontal headaches and attacks of dizziness. There was also a moderate rise in temperature, to about 101 F., which persisted for the first three days. This was followed by a gradual but constant decline in her condition. She became more dull and apathetic, and at the end of two weeks sank into a deep coma,

from which she could not be aroused, although she swallowed food when it was poured into her mouth. She remained in this condition for about six days, and then regained the earlier state of apathy and semistupor with brief lucid intervals when she would talk coherently. In a few days she again became comatose and remained so for two days, her condition then cleared up partially. At no time during this whole period was there noticed any loss of power, convulsions or twitchings. There was no complaint of diplopia. During the periods of stupor, she was incontinent of urine and markedly constipated. Imme-

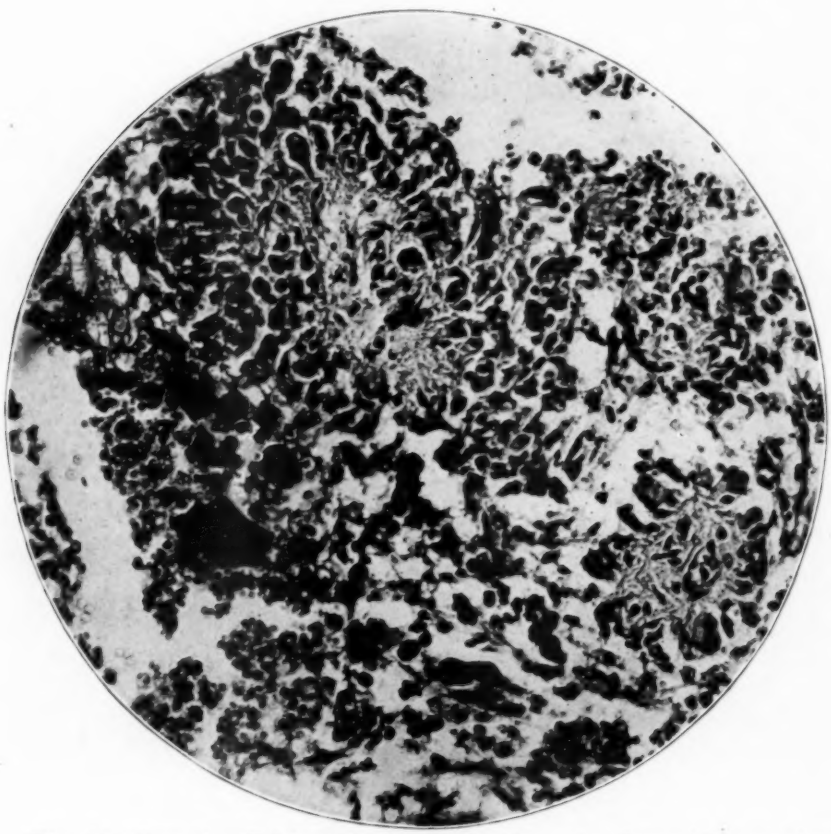


Fig. 13 (Case 6).—Fairly typical field showing roset formation and giant cells.

diately after admission the patient lapsed into coma. At this time there was no paralysis; the pupils were contracted, they reacted to light sluggishly; the jaw reflex was increased; the biceps and triceps were equally active; the abdominals were not elicited. The knee jerks were not obtained, the ankle jerks were diminished; and there was a bilateral Babinski, more marked on the right than on the left.

On the following day, the patient's condition began to clear up, but she was still confused and manifested evidence of motor aphasia; she carried out commands but could not formulate answers. At this time, in addition to the previous findings, a right central facial paralysis developed.

On May 15, the knee reflexes were diminished. The diagnosis of left frontal neoplasm was suggested, but in view of the multiplicity of symptoms, progressive softening or encephalitis was also considered.

Examination.—Repeated examinations of the fundi failed to disclose any involvement of the disk. Repeated examinations of urine showed a faint trace of albumin. Blood chemistry: showed urea nitrogen, 22.4; incoagulable nitrogen, 51.2; uric acid, 3; creatin, 1.3; sugar, 0.14 and carbon dioxid, 14.1. The Wassermann test was negative on blood and cerebrospinal fluid. The fluid was clear and contained no cells. A roentgenogram showed the sella turcica eroded posteriorly, the posterior clinoid process completely destroyed and the grooves for the meningeal vessels increased in depth. In the left parietal region, there was an irregular oval shadow measuring about 1 to 4 inches in long diameter, which runs transversely. It was impossible to state whether this was within the skull or in the cranial bones.

Course.—Because of the uncertainty in diagnosis, ventriculography was suggested, but could not be carried out, as there was a rapid decline in the patient's condition. Deep stupor ensued, with a rise in temperature and signs of hypostatic pneumonia which led to a fatal issue on May 30.

Gross Anatomy.—The surface of the brain showed evidence of increased intracranial pressure. On the orbital surface of the right frontal lobe there was a yellowish-white discoloration of the cortex.

On section, 1 inch posterior to the frontal pole a tumor mass was found in the left hemisphere, involving almost the entire white substance. A similar mass was found in the right hemisphere, but this was more vascular and presented a large hemorrhage in its lateral aspect (Fig. 14). The tumor mass itself was also highly vascular, presenting a honeycomb appearance with numerous small cysts. The two masses could be traced posteriorly as two independent tumors for a distance of 2 inches (5 cm.) with the right mass extending somewhat more dorsally and laterally, involving at its posterior extremity the dorsal portion of the internal capsule and the adjacent portion of the corpus striatum. The left extended ventrally and somewhat mesially, infiltrating almost completely the lenticular nucleus and adjacent portion of the island of Reil. Both tumor masses were surrounded by fairly wide zones of edema.

Microscopic Anatomy.—Sections of tumors presented a typical picture of spongioblastoma. It does not require further description as it corresponded in almost all details to the cases already described.

CASE 8.—*History.*—F. S., aged 47, admitted to the hospital, Oct. 30, 1924, gave a history of frequent headaches during the past year. Four weeks before, while getting breakfast, she suddenly cried out, lost consciousness, fell to the floor, foaming at the mouth, with eyes rolling, gritting of teeth and incontinence of urine. There were no convulsive movements. This condition lasted fifteen minutes. Recovery was complete. The next day she appeared somewhat dazed, and complained of weakness in the right side. On the third day, while shopping, she began to tremble. She was taken home in a dazed condition and examined by a physician, who found weakness on the right side. Then there followed a free interval of two weeks, until the day before admission to the hospital, when weakness increased, and the patient became restless and incontinent.

Examination.—Examined in the hospital, the patient was somewhat euphoric, confused, disoriented and amnesic. The pupils were equal, and reacted to light

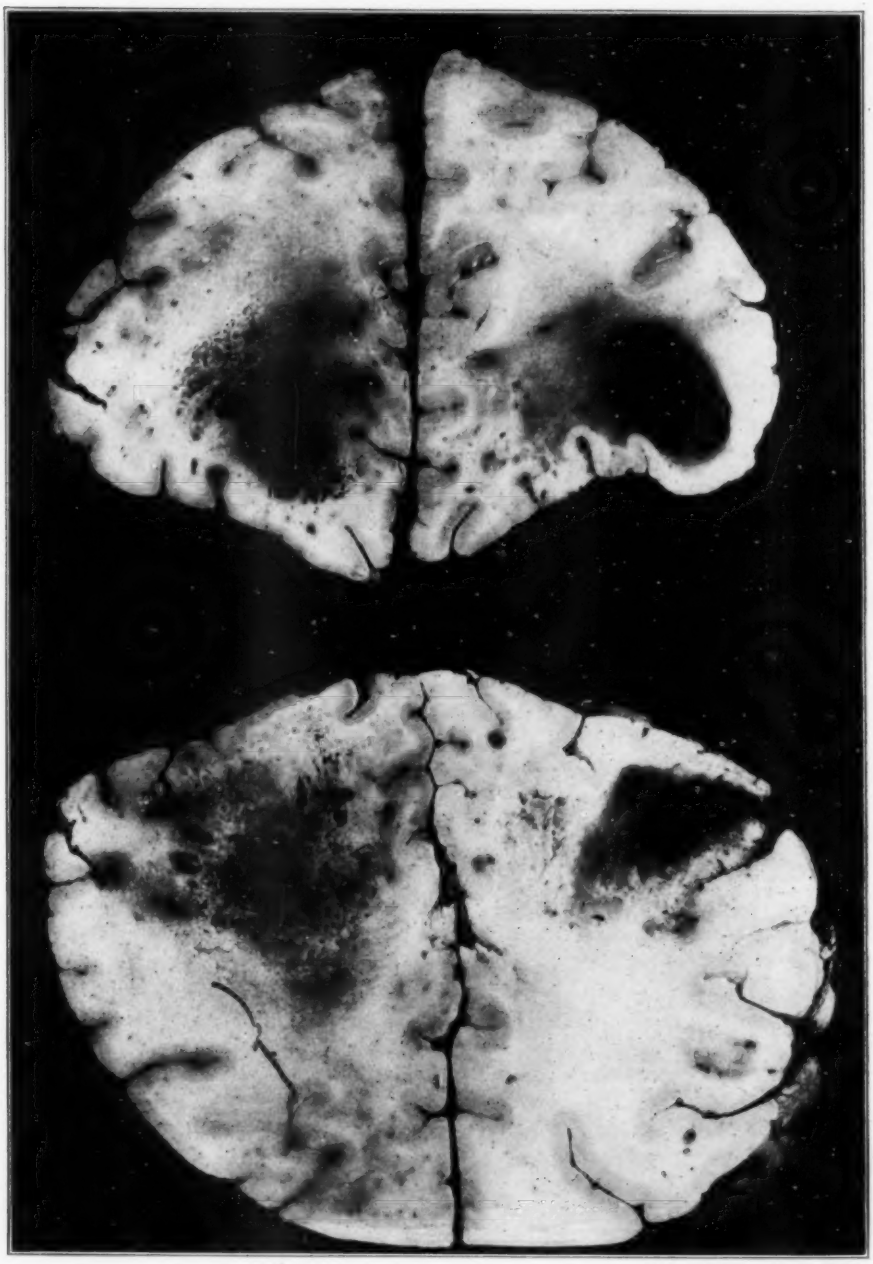


Fig. 14 (Case 7).—Multiple centers of tumor growth in Case 7.

and in accommodation. There were right ptosis and right hemiparesis. The tongue deviated to right. The fundi showed arteriosclerotic changes. Lumbar puncture was negative, with normal pressure and contained no cells. Blood pressure was: systolic, 118, diastolic, 70.

Course.—The patient's condition gradually declined, with periods of alternating stupor and alertness, but without change in the objective symptoms, and death occurred, November 28.

In this case the diagnosis lay between thrombosis and progressive softening due to arteriosclerosis or a neoplasm. In the beginning the first diagnosis was favored, but later a diagnosis of cerebral tumor was made.

Gross Anatomy.—The pia-arachnoid appeared dull, particularly over the frontal lobes. In the left frontal lobe over an area corresponding approximately to about the middle one-third of the superior and upper intermediate frontal gyri, there was a peculiar change in the appearance of the leptomeninges and the underlying cortex. The former had the appearance of a scar, was glistening and presented a yellowish-gray hue; the latter was somewhat firmer in consistency and on incision presented a tumor whose cut surface was granular and dirty gray, with small hemorrhagic foci.

The tumor extended from about 1 cm. from the frontal pole backward as far as the anterior limit of the island of Reil. It was oval in outline and was limited to the superior frontal convolution. It was, however, surrounded by a wide zone of edema which included almost the entire frontal lobe on this side. The tumor mass was highly vascular (Fig. 15).

Another neoplastic mass was present in the region of the lenticular nucleus (Fig. 16).

Microscopic Anatomy.—Here the histologic features differed from those of the other tumors in that the giant cells were not so numerous, and the most common form of cell was the fusiform and flask-shaped. Rosets were seen only occasionally. Cystlike structures and palisade formations were the more conspicuous features.

Case 9.—*History.*—J. I., aged 5, admitted to the hospital, Jan. 30, 1924, one month before fell down stairs striking the back of his head. Since then he had complained of persistent severe headache. Immediately after the injury, the patient was unable to walk. Recently, however, he had begun to walk a little. There was also bilateral ptosis of the upper eyelids for a few days after the injury. The fall was not associated with loss of consciousness. The patient vomited once one day after the accident and again on the day of admission to the hospital. Recently a tremor in the right hand was noticed by his mother.

Examination.—The patient apparently was normally developed mentally, for his age. He was somewhat drowsy. His head was large. Vision was good on the right side, but poor on the left. There was bilateral papilledema. The right pupil was larger than the left; their reactions were poor. There was a bilateral weakness of the external rectus and right internal rectus. There were nystagmoid twitchings and ptosis on the left. There was corneal hypesthesia on the left side, and left central facial weakness. The deep reflexes were more marked on the left than on the right. The left abdominal reflexes were not obtained. There were a Babinski reaction and ankle clonus on the left. The left arm and leg were weaker than the right. There was slight ataxia on the right side, more marked on the left, and adiadokokinesis was more marked on the left than on the right.

The impression was gained that the case was one of cerebral neoplasm, probably of the right frontal region, with secondary cerebellar symptoms due

to pressure or to internal hydrocephalus resulting from obstruction of the aqueduct of Sylvius by a neoplasm. The trauma suggested also the possibility of a very slow middle meningeal hemorrhage. The spinal fluid showed two cells per cubic millimeter.

Ventriculography was performed with the needle inserted into the left occipital lobe, and a tumor was encountered. The roentgen ray showed dilated

Fig. 15 (Case 8).—Character and location of tumor mass.

ventricles, the left posterior horn oblitered and the posterior half of the third ventricle occluded.

Course.—Death occurred, February 9, twelve hours after ventriculography, due to puncture through the tumor and consequent hemorrhage.

Gross Anatomy.—The surface of the brain showed evidence of increased intracranial pressure. Over the right frontal region there was an area of subpial hemorrhage about 2 inches (5 cm.) in diameter. The brain was soft

and somewhat collapsible, suggesting an internal hydrocephalus. In the left occipitoparietal region, the cortex was particularly friable. Beneath it, there was a large diffuse neoplastic mass; it was dark red on the surface, but deep in its substance it had a pearly gray appearance (Fig. 17). It differed in

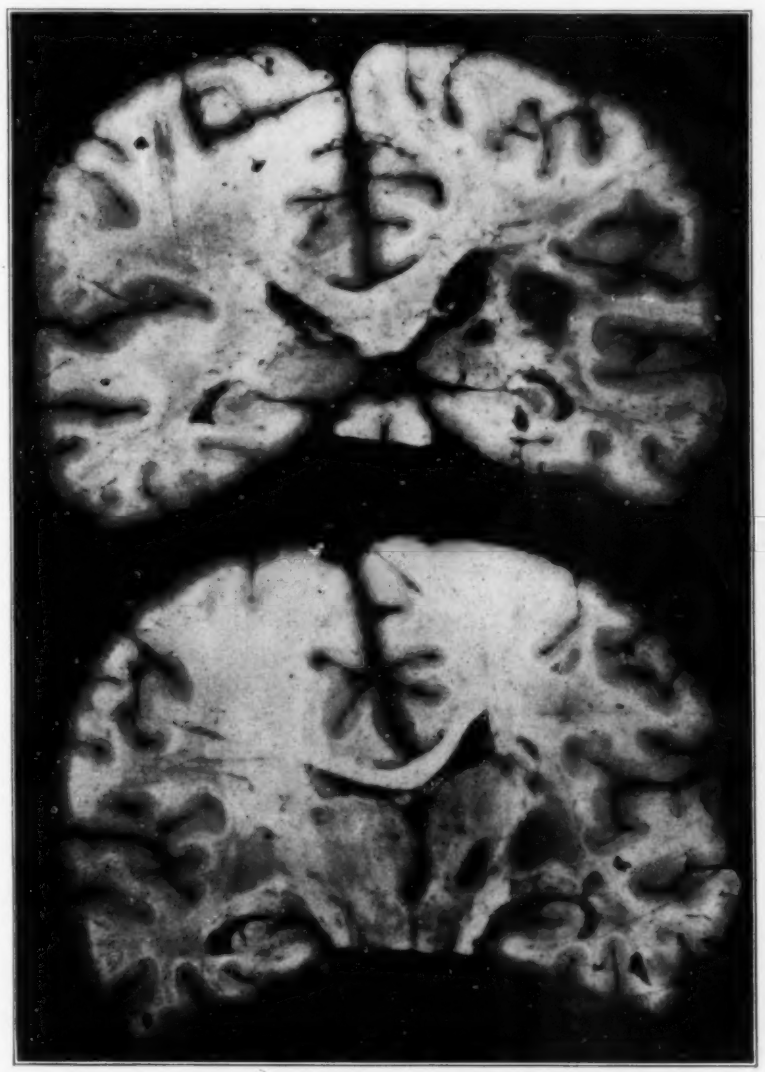


Fig. 16 (Case 8).—Another center of growth in the lenticular nucleus.

consistency in various regions, being friable in the hemorrhagic and deeply colored area, but hard in the pearly white zone. On horizontal section of the brain, the tumor mass was found to involve almost all of the white matter of the parieto-occipital lobe, compressing and dislodging the posterior and descending horns of the lateral ventricles forward. By its growth forward from the

occipital region, it herniated so as to compress the midbrain, in this way obstructing the aqueduct of Sylvius, resulting in marked internal hydrocephalus in both lateral ventricles. Anteriorly the growth invaded the temporal lobe. Another tumor mass was found on the left side, involving the midbrain.

Microscopic Anatomy.—A large number of sections taken from various portions of the tumor and adjacent brain tissue showed a fairly uniform picture. The background consisted of numerous flask-shaped, fusiform and rounded cells, rich in protoplasm and endowed with large vesicular nuclei. In places these cells tended toward nest formation suggesting rosets, and in others they were arranged radially about blood vessels. In several fairly well circumscribed areas there were groups of cells which formed elliptical collars about necrotic centers. They were four to five cells deep and were of a rapidly growing type. Many of these cells appeared to send out fine processes which were

Fig. 17 (Case 9).—Extent and appearance of tumor.

directed toward the necrotic centers. The tumor was highly vascularized and numerous hemorrhagic areas were seen throughout the microscopic field. In a few isolated areas there was a deposit of calcium around blood vessels. The general impression was that of a highly proliferative neoplasm, glial in origin, with many growth centers, which were typical of spongioblastoma. There were, however, other areas in the growth in which the cells exhibited a little further advance in the process of differentiation, approaching more nearly the morphology of astrocytes.

Case 10.—*History.*—E. M., admitted to the hospital, Dec. 31, 1923, eight months prior to admission had difficulty in writing. This became progressively worse, and three months later there followed impairment in his ability to play the zither. At this time, he began to have occasional attacks of unprovoked crying, and other evidence of emotional instability. The following month he developed weakness in the right arm, and vomited three or four times. For several months before the onset, he had been unusually irritable.

During the early part of November, while bowling, the patient slipped and fell several times. Within a few days he noticed some weakness of the right arm, and his weakness progressively increased. He also developed occasional difficulty in speech which during the week before admission had become more markedly impaired. In addition, during the last week the weakness of the right side had developed into a complete right hemiplegia, accompanied by a complete loss of the power of speech. During the twenty-four hours prior to admission, convulsive attacks developed. These were jacksonian in character, beginning in the right arm and spreading to the right side of the face and right lower extremity. On the day of admission, these attacks became frequent, occurring as often as once in fifteen minutes. At no time did the patient complain of headache, nor did he vomit.

Examination.—The patient was drowsy. He understood spoken language and carried out orders, but could not talk. During the examination, he had a convulsive seizure which began in the right arm and spread to the right side of the face and then to the right lower extremity. His reflexes showed general hyperreflexia. There were right ankle clonus, and a bilateral Babinski sign; the abdominal and cremasteric reflexes were absent. There was complete paralysis of the right upper and lower extremities, with slight spasticity. The sensory status could not be evaluated. The pupils were equal. The fundi showed slight blurring but no measurable swelling. There was paralysis of all branches of the facial nerve. There was slight deviation of the tongue to the right, slight rigidity of the neck and a bilateral Kernig sign. On percussion, the left temporal region was tender. A roentgen-ray examination was reported negative. The spinal fluid was under increased pressure and contained six lymphocytes per cubic millimeter. The Wassermann tests of the blood and spinal fluid were negative. The urine was normal. A preoperative diagnosis of slowly increasing venous extradural hemorrhage or hemorrhage into a neoplasm was made. Craniotomy was performed, December 31, and a deep left cerebral neoplasm was found. Following the operation the temperature increased rapidly, reaching 105.4 F. on the fifth day, Jan. 5, 1924, on which day the patient died.

Gross Anatomy.—The surface of the brain showed evidence of increased intracranial pressure. On separating the hemispheres, a distortion of the corpus callosum by a tumor projecting through it was seen. The left side of the brain appeared larger than the right. On section of the brain a large tumor of the left frontal lobe was seen (Fig. 18). The tumor extended forward to within 5 cm. of the anterior pole and 4 cm. from the lateral margin of the brain. It invaded both sides of the corpus callosum at the genu and for a short distance back. The tumor measured about 8 by 5 by 4 cm. It was yellowish-red on fresh section and not encapsulated; another small tumor mass was seen in the other hemisphere in the subependymal structure close to the outer wall of the descending horn of the lateral ventricle. There were a few streaks representing the lines of operative punctures and a few areas of fresh hemorrhage surrounding them.

Microscopic Anatomy.—Sections of the tumor mass and adjacent cortex showed the neoplastic process to involve mainly the subcortical tissue and only in a few regions to infiltrate the overlying cortex. The tumor mass was more or less uniform in its cellular make-up, the cells were mainly of a fusiform type, giving off fairly long processes and containing elongated nuclei rich in chromatin. Many of the nuclei showed amitotic figures. Occasionally small masses of rounded cells were found in an arrangement not unlike roset forma-

tion. In some areas there were what appeared to be ependymal cyst formations, and in others, a palisade arrangement of glial elements. There were striking proliferative changes about blood vessels throughout the mass. They apparently involved the adventitial structures. The latter were seemingly the seat of elaboration of large epithelioid cells, with the formation of thick perivascular coats or sheaths. These cells contained many amitotic figures and were in the process of progressive proliferation.

Case 11.—*History.*—S. R., aged 65, admitted to the hospital, Feb. 28, 1924, in April, 1923, sustained an injury to his head and was dazed for a brief period of time. A few weeks later, he began to complain of dimness of vision and pain in the eyes. Glasses were prescribed, but without benefit. He began to show signs of irritability and garrulousness. About four months before admis-

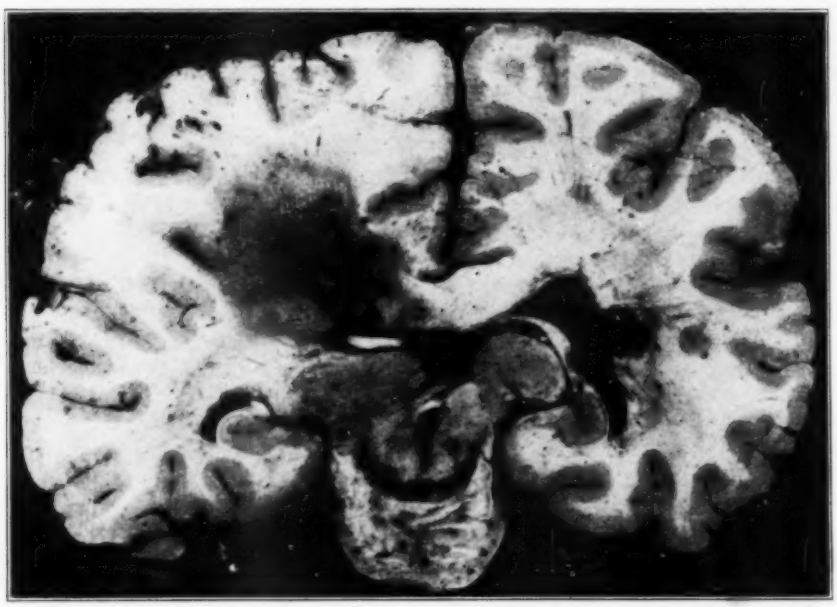


Fig. 18 (Case 10).—Main tumor mass and a small independent neoplastic growth in the opposite hemisphere bordering on the lateral ventricle.

sion, the patient began to experience difficulty in finding proper words to express his thoughts; he also began to complain of failing memory. His irritability became more pronounced. He began to show other changes in conduct and in emotional reactions, he became suspicious, delusional and unclean in his habits. Speech, memory and ability to write and read gradually became more defective. More recently, during the last three weeks, a weakness in the right arm and right leg had developed, and speech had been almost completely lost.

Examination.—On admission, the patient appeared apathetic and deteriorated. He had an enlarged heart and a diastolic murmur at the base. The blood pressure was: systolic, 140; diastolic, 80. There were aphasia, alexia, agraphia and apraxia. The disks showed mild papilledema, more marked on the left than on the right. The pupils were irregular and sluggish to light. There were slight bilateral ptosis and right facial weakness. The deep reflexes were

hyperactive, more marked on the right than on the left. The abdominal reflexes on the left were more marked than on the right. There was weakness and spasticity of the right leg and arm. Caloric examination indicated no lesion of the eighth nerve or in the posterior fossa.

The Wassermann test of the blood was negative. Lumbar puncture gave a clear cerebrospinal fluid containing 8 lymphocytes to the cubic millimeter. The Wassermann and colloidal gold tests were negative.

Course.—From the day of admission there was a gradual decline in the condition of the patient. He became more stuporous, and there developed a Babinski sign on the right side.

The diagnostic possibilities considered were a vascular lesion or a neoplasm in the left temporosphenoidal lobe.

Exploratory craniotomy was performed, and the left frontal area was investigated. There was a slight increase in pressure. No tumor was seen. The brain was yellowish, probably owing to softening resulting from pressure by deep-seated neoplasm. Death occurred two days after operation, March 13.

Gross Anatomy.—The pia-arachnoid was somewhat dull and presented an area of discoloration in the region of the superior and middle frontal gyri on the left side. There was moderate atheromatous change in the vessels at the base. The gyri were somewhat flattened, particularly on the basal surface of the left hemisphere. The hippocampal and fusiform gyri on that side were markedly increased in consistency.

On incision at the level of the genu of the corpus callosum and somewhat posterior to it, there could be seen some distortion of the ventricle, especially on the left. In a section at the level of the trigonum olfactorium there was seen in the left hemisphere the anterior extremity of a grayish neoplastic mass, which measured 2 cm. in diameter and which was fairly well circumscribed. It was situated mainly in the temporal lobe, displacing the structure median to it, and compressing the lateral ventricle of the same side to the left. The third ventricle was also deformed with its convexity to the right.

Sections at the level of the corpora mamillaria showed the temporal lobe almost completely replaced by a tumor mass, leaving only a narrow zone of the cerebral hemisphere about it, which retained a relatively normal configuration.

The tumor mass could be traced back throughout the parietal lobe and invaded the anterior part of the occipital lobe for a short distance (Fig. 19).

Microscopic Anatomy.—Beside the histologic features common to the tumors already described, this growth presented in several areas a large number of fusiform cells so arranged as to give the tumor an appearance of a myxomatous growth (Fig. 20). This type and arrangement of cells has led to the use of the term myxoglioma for growths of this kind.

CASE 12.—*History.*—C. P., aged 28, admitted to the hospital, Oct. 9, 1923, about two years before began to have frontal headaches, which extended to both temporal regions. They became progressively more frequent, and for the last four days had been almost continuous and more severe than ever. In April, 1923, there was a jacksonian attack confined to the left side of the face. In July, a jacksonian attack extended to the left arm. In August, a severe jacksonsion epilepsy started in the face, spread to the arm and leg, and became generalized. There were no changes in the disks at this time. For the last four days the patient had been nauseated but had not vomited. Six months before, the patient noticed twitchings on the right side of the face. These twitchings disappeared two months ago, but at this time he noticed weakness

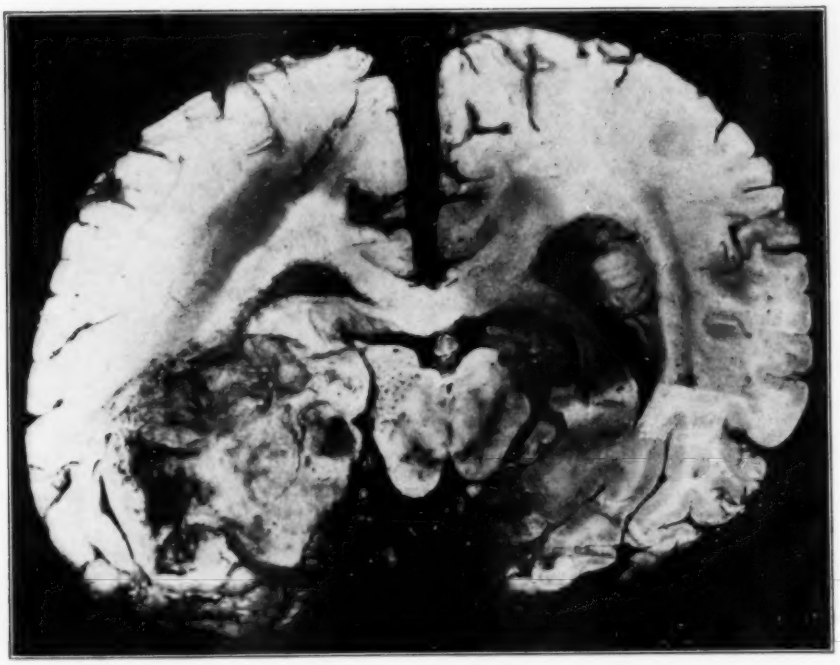


Fig. 19 (Case 11).—Tumor mass; note the hemorrhagic and the cystic character of the tumor.

Fig. 20 (Case 11).—A selected area showing the fusiform cells which give the appearance of a myxomatous growth.

of the same side of the face, and food would occasionally fall out of his mouth. There was also difficulty in chewing food. Three weeks prior to admission, there was progressive weakness of the left arm and hand and impairment of vision.

Examination.—There was weakness of the left shoulder, elbow and wrist, most marked in the wrist, and some weakness in the left lower extremity. The facial weakness on the left was more marked in the lower branches, but also involved the upper branches. The triceps, radius, suprapatellar, patellar, Achilles, and cremasteric reflexes were more active on the right than on the left. There was a Babinski sign on the right. The lower abdominal reflexes were more active on the right than on the left. There were no sensory changes. The pupils were equal and reacted promptly to light and in accommodation. There were no ocular palsies. There was no change in the visual fields to gross tests. There was bilateral early papilledema. Caloric examination was normal. Diagnosis: Neoplasm in the right prerolandic area.

Course.—On October 16, a craniotomy was performed under local anesthesia. A large infiltrating tumor was found in the cortical and subcortical tissue, which was not favorable for removal. Ten hours after operation the patient became comatose and died within twenty-four hours (Oct. 17).

Gross Anatomy.—On incising the dura a large protruding hemorrhagic and necrotic area was exposed. It was dark and friable. This lesion extended for 2 cm. in front of the central fissure and about 1.5 cm. posterior to it. Its lower border almost reached the Sylvian fissure, while its upper border extended up to the level of the lower half of the second frontal convolution. Its edges were not, however, well defined. The convolutions around this lesion were widened and flattened, and the sulci were definite shallow. The whole anterior half of the right cerebral cortex felt soft. A cut section of the brain on the level of the neoplasm showed a striking resemblance to the neoplasm in Case 6 (Fig. 21).

Microscopic Anatomy.—Section through the tumor mass presented a very cellular structure. The cells were highly proliferative in character and contained a small amount of cytoplasm and vesicular nuclei which took a deep hematoxylin stain. Mitotic figures were frequently seen. A large number of cells were seen with nuclei arranged at the periphery forming a complete circle of overlapping nuclei. In general, the cells had a tendency toward nest formation; a tendency to roset formation was also noted. The tumor cells occasionally radiated about blood vessels and infiltrated the adjacent brain tissue.

Case 13.—*History.*—R. R., aged 55, admitted to the hospital, March 15, 1923, three weeks prior to admission experienced a lapse of memory. Since that time he had experienced difficulty in thinking and in expressing himself, and he easily became fatigued by attempts to speak. He suffered with headaches, which were becoming progressively worse, keeping him awake at night. With this there occurred frequent attacks of vomiting, forceful and projectile in character. More recently there was a sudden impairment in vision, with occasional attacks of diplopia.

Examination.—The patient was a man past middle age, fairly well developed and well nourished. His intellect apparently was unimpaired, his speech was somewhat slurring, his gait was unsteady, and he walked on a broad base. He staggered to the right, but no apparent ataxia or incoordination was brought out by finer tests. There was diminution in visual acuity with the field of vision on the right side contracted. Both pupils reacted well to light and in accommodation. There was bilateral external rectus weakness, the

right greater than the left, and bilateral papilledema. There was left peripheral facial weakness. The upper deep reflexes were exaggerated, more marked on the right than on the left. The abdominal reflexes were present, although the right was diminished. The lower deep reflexes were exaggerated, more markedly on the right than on the left. There were no pathologic reflexes.

At this time the diagnoses of multiple lesions and of left frontal neoplasm at the base of the brain were considered.

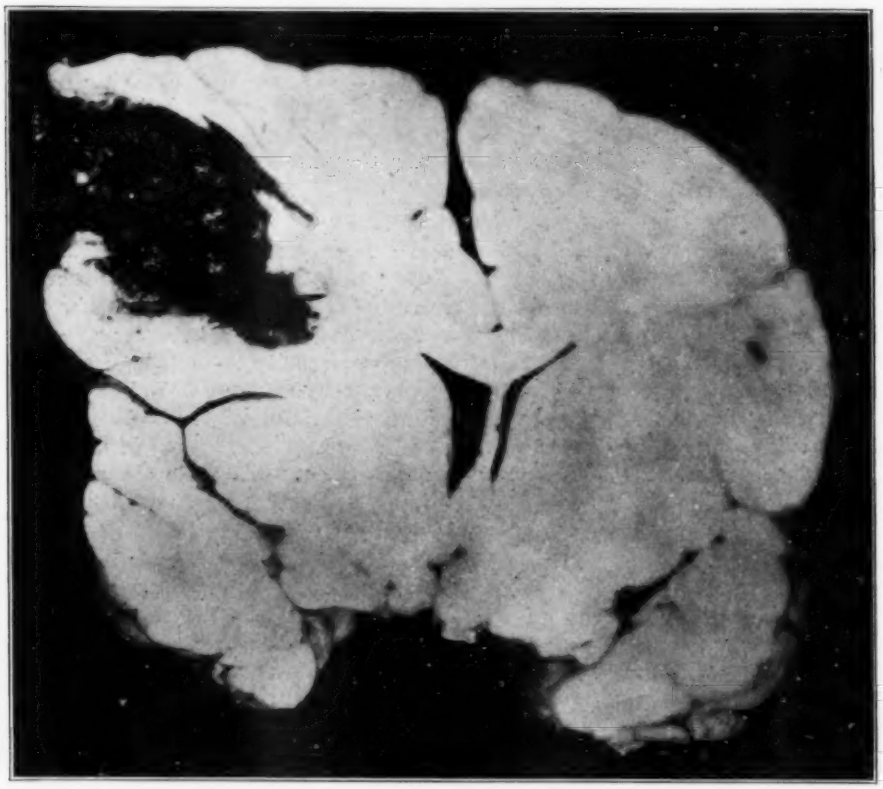


Fig. 21 (Case 12).—Marked vascularity of neoplasm in Case 12. Compare with Figure 12 and note striking similarity.

Course.—On March 15, lumbar puncture was performed. The fluid was under normal pressure, had a faint yellow tinge, but showed no gross blood. Microscopically, there were a few red blood cells, 4 lymphocytes per cubic millimeter and increased globulin. On March 31, a ventricular puncture was performed in the right occipital region. The ventricle was found with difficulty. The fluid was not under pressure; 25 c.c. were withdrawn and 15 c.c. of air were injected.

Roentgenograms did not yield any definite localizing evidence.

Three days after the ventriculography there was almost complete loss of vision, with the papilledema reaching about 4 diopters in each eye. Because of these findings, craniotomy was decided on and was performed under local anesthesia. Exploration did not disclose evidence of a neoplasm. The presence of congestion of the pial vessels suggested the possibility of an inflammatory lesion. Three days after the operation there was partial return of vision.

Subsequently, a gradual decline in patient's condition occurred with increase in the papilledema, the gradual development of coma, paresis of the left upper extremity and the appearance of a left Babinski sign; right facial weakness (central type) and ptosis of the right eyelid.

The patient died on May 29.

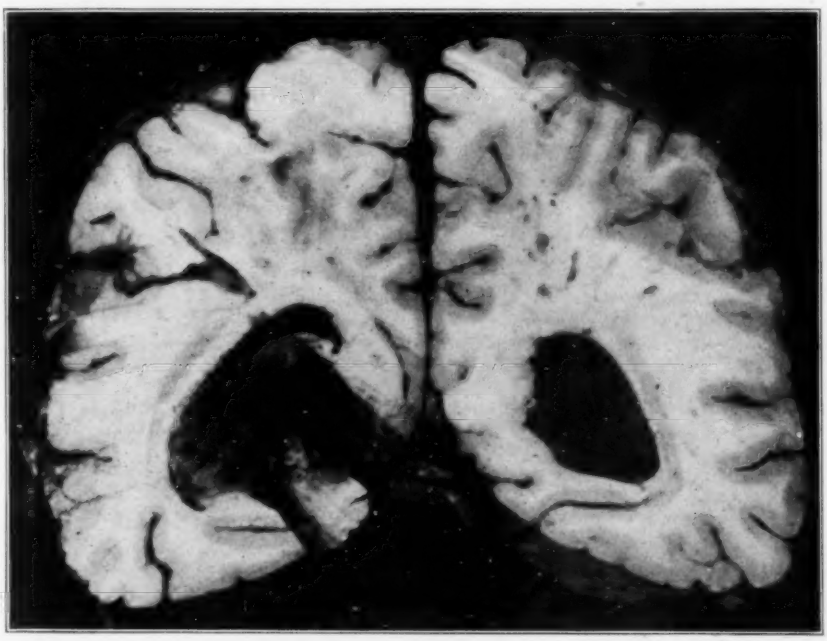


Fig. 22 (Case 13).—Marked vascularity and localization of the main tumor mass.

Gross Anatomy.—The brain showed evidence of increased intracranial pressure. There was no hemorrhage or exudate on the surface of the brain. The base of the brain and cranial nerves were undisturbed. The right lobe of the cerebellum felt cystic. On section, the ventricles in the anterior part of the brain were found to be moderately and symmetrically dilated. Between the left inferior horn and the body of the left lateral ventricle there was an infiltrating tumor, measuring about 5 by 3 by 3 cm., which compressed the left inferior horn and the body of the left lateral ventricle, and which distorted by compression the body of the right lateral ventricle. The tumor pressed on the posterior part of the thalamus, the pineal gland and the posterior part of the third ventricle. It was reddish yellow (Fig. 22). Section at the level of the anterior commissure disclosed another small tumor mass on the mesial surface of the left frontal lobe (Fig. 23).

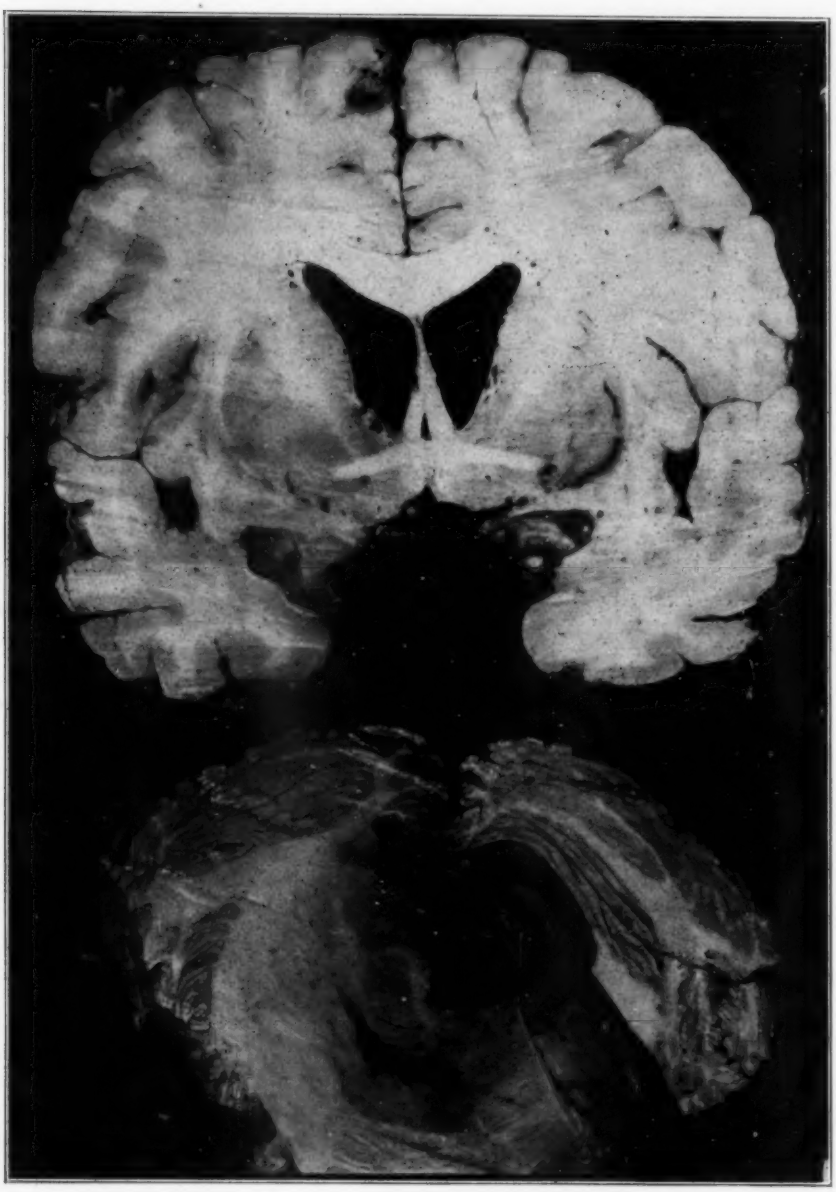


Fig. 23 (Case 13).—Two additional centers of growth.

On sectioning the cerebellum, a large cyst measuring about 3 by 2.5 by 2.5 cm. was found in the right cerebellar lobe extending a short distance across the midline. The cyst had a definite membrane supplied with blood vessels and could be separated from the substance of the cerebellum. The membrane was about 2 mm. in thickness. The cyst cavity was partly filled with dark brown, soft friable material (Fig. 23).

Microscopic Anatomy.—Sections from the main neoplastic mass presented features of a highly cellular new growth in type and arrangement not unlike

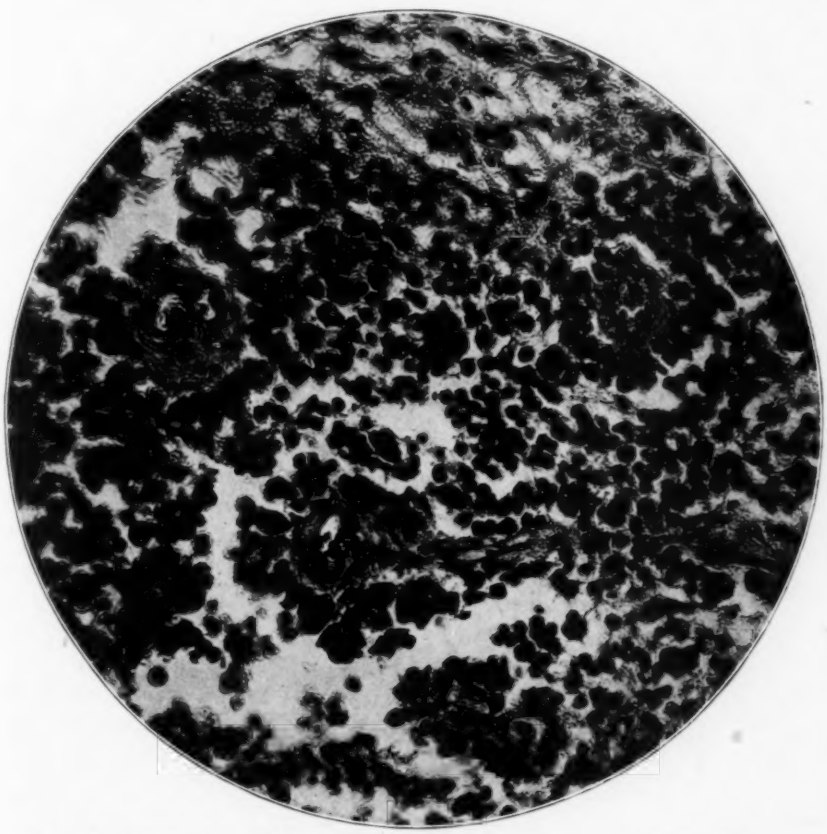


Fig. 24 (Case 13).—Epithelial character of cells and their tendency to cluster about blood vessels.

those seen in spongioblastoma. The majority of the cells were large, irregular in outline and epithelial in character, with large nuclei rich in chromatin material arranged in the form of small alveoli or small radially grouped masses (Fig. 24). Occasionally they assumed the form of ependymal cysts, with cells arranged in radiating fashion about them (Fig. 25). Scattered among the cells were numerous giant cells (Fig. 26). The latter were characterized by the peripheral arrangement of nuclei and some of them had the appearance of rosets. In various parts of the tumor there were variations from these types and general arrangements. In some areas typical astrocytes were seen.

A section of the wall of the cyst in the cerebellum showed the latter to be invaded by cells similar in type and arrangement to those found in the main tumor mass. This cyst was looked on as a degenerative area in a secondary growth center.

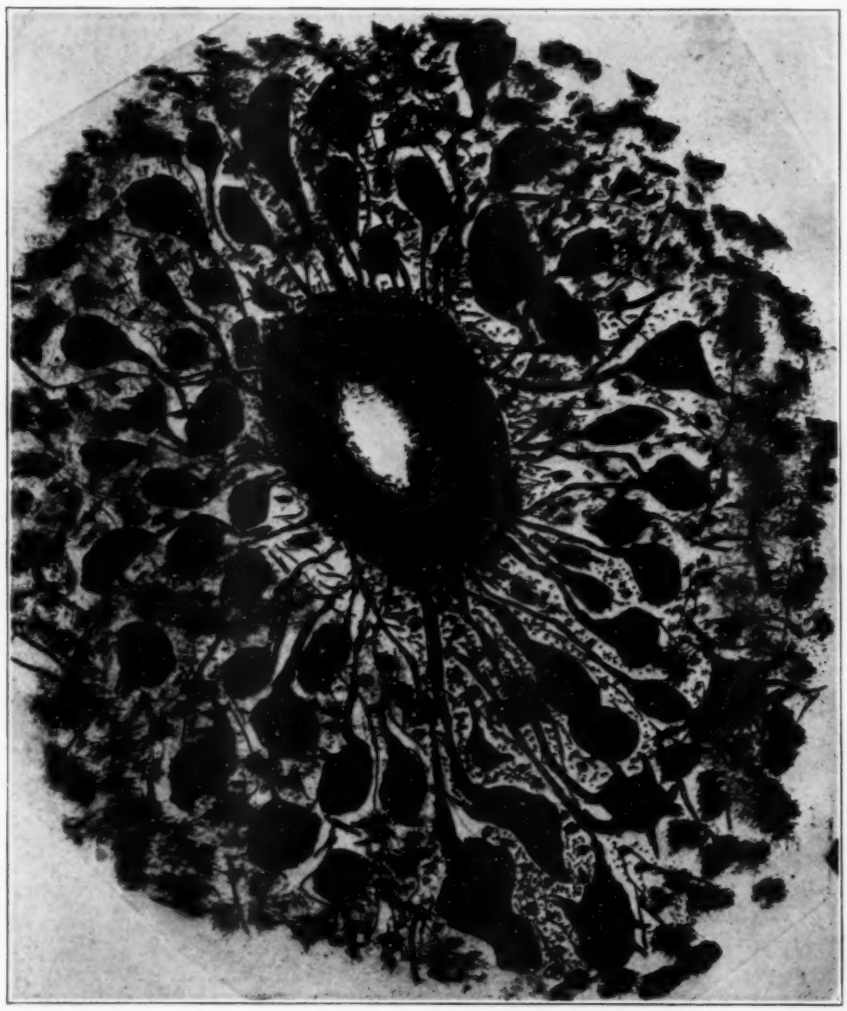


Fig. 25.—Camera lucida drawing, showing character of the glia cells and their radial arrangement (Gold-sublimate method; compare with Figure 24. Zeiss ocular, 6 ×; objective, 166 mm.).

Case 14.—H. G., aged 22, admitted to the hospital, March 21, 1923, at the age of 1 fell and struck his head over the left eye, causing a bad cut. Five years ago a trapdoor fell on the patient's head, but did not cause loss of consciousness nor cut the scalp. The present illness began two years before admission, with a transient attack of blurred vision. About two months later he began to have sharp pain in the left eye, which came on in daily attacks

lasting several hours. These attacks persisted for about six weeks. At this time the patient consulted an eye specialist, and was told that there was a hemorrhage in the left eye. There was also albumin in the urine. He was given medication; the pain disappeared, and the patient was free from symptoms for about six months. Then for a period of four weeks, frontal headaches and blurred vision reappeared. At this time there occurred an internal strabismus (the left eye turned in), which was associated with double vision. There was no rise in temperature and no evidence of constitutional disorder, and the symptoms disappeared spontaneously. Again he remained free from symptoms for a year, when once more he began to suffer with frontal headaches. These

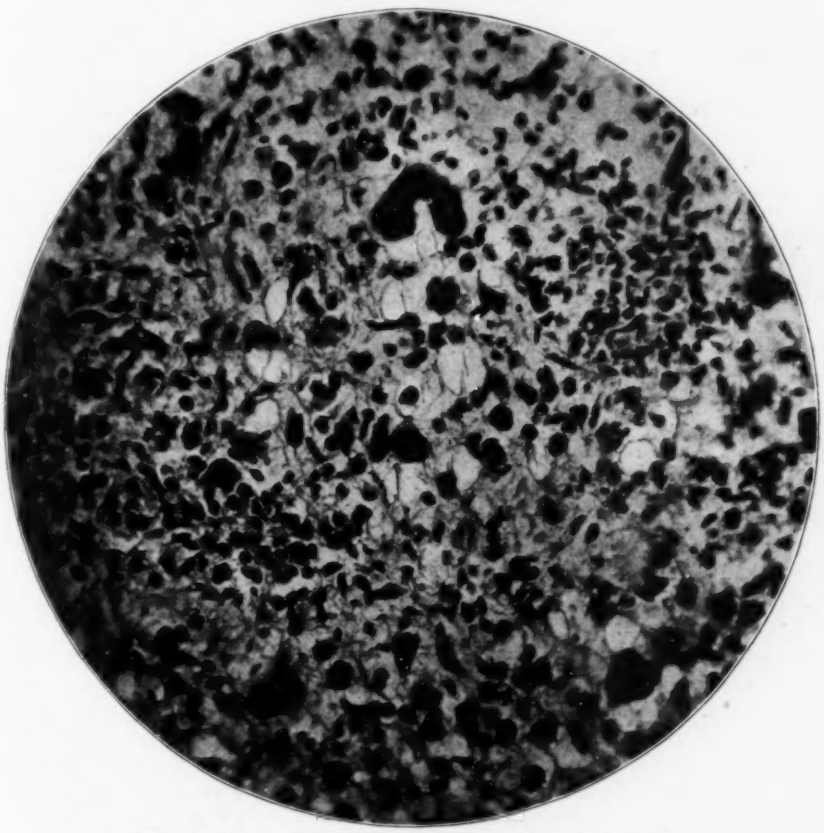


Fig. 26 (Case 13).—Giant cells and roset formation.

now remained constant, and during the last two months he had complained of paresthesias of the face, such as crawling, numbness and a feeling of lightness, not confined to one side but more frequent on the left. There were also blurred and double vision, with the left eye turning out and numbness of the left side of the tongue and left side of the nose. Practically all these symptoms disappeared at the end of one month. During this period, the patient was at the Neurological Institute where the diagnosis of brain neoplasm was made. Roentgen-ray examination and blood tests were negative. For the past two weeks, the patient had noticed a flattening of the left side of the face and

pain in the right lumbar region. More recently there had been short periods in which he had had mild difficulty in speech, using the wrong words, though he knew the word he wanted to use and was aware of the mistakes he made. A month ago, the patient vomited once without nausea. There had been no vertigo at any time and no deafness, tinnitus or disturbances of gait or station. There had been no convulsions, no hallucinations of vision and no cardiorespiratory symptoms.

Examination.—Station and gait were normal. Power was good, and coordination tests were negative. There was no tremor, no ataxia, no adiadiokokinesis and no abnormality in the cheek reflex. There was no spontaneous past pointing in the vertical or horizontal planes and no asynergy of trunk, shoulder or pelvic girdle. The jaw, pectoral, triceps, wrist, suprapatellar, patellar, Achilles, abdominal and cremasteric reflexes were equal. The biceps reflex was more active on the right than on the left. There was no Babinski sign. There was no objective sensory disturbance. Vibratory and joint senses were intact. There was no astereognosis. The cranial nerves were negative except for bilateral choked disks; there was fine nystagmus in all directions, slight bilateral exophthalmos and definite atrophy of the masseter and temporal muscles on the left side. The patient was cheerful, intelligent, and no speech disturbance was noticed.

Ear examination showed hearing normal in both ears. There was nystagmus directed to the right only on extreme lateral fixation of the eyes to the right. There was no spontaneous past pointing. Caloric stimulation of the left vertical canals met with a prompt response so far as nystagmus was concerned. There was subjective vertigo, but no past pointing. Because of symmetry of loss in past pointing reaction and the presence of nausea and vomiting on caloric stimulation of both sides, there was considered to be no lesion in the posterior fossa.

Course.—On March 30, a ventricular puncture was performed. The anterior and posterior horns of the ventricles were markedly distended, but the outlines were regular. There was a defect in the body of the right lateral ventricle which had such an appearance as would be produced by pressure of a deep tumor in the right centrum semiovale or a tumor arising somewhere in the brain stem and exerting pressure forward. Study of plates suggested that the neoplasm lay near the posterior portion of the third ventricle, probably more on the left side, or on the outside of the third ventricle to the left.

On April 18, bilateral papilledema was more marked; nystagmus was as before. There was inequality of the pupils, slight left ptosis and distinct weakness of the left internal rectus. The exophthalmos was more marked and there were bilateral corneal hypesthesia, bilateral diminution in hearing and slight right facial weakness (central). There was no Babinski sign. The left knee reflex was more marked than the right.

On April 25, the patient left at his own request, but promised to return for further study and treatment. The urine, blood and spinal fluid Wassermann were negative.

On May 19, the patient was readmitted. The interval history indicated failing vision, intense headaches and pain in the left suprascapular region radiating to the left breast, causing a sensation of muscular fibrillation. The papilledema was less marked as postneuritic atrophy was setting in.

On May 25, a ventriculography was performed, and the entire ventricular system was dilated. There was a defect in the body of the right ventricle due to a tumor of considerable size bulging into the ventricle and seemingly attached

above and to the right. The right ventricle was more dilated here than the left and was dislocated.

On May 29, a two stage craniotomy was performed. A tumor was found in the body of the right lateral ventricle. Fragments were removed for diagnosis. There was bleeding, and the wound was closed to be opened again. In the second stage a great portion of the tumor was removed.

The general condition after operation was as good as before. The fundi oculi remained unchanged. A week following the operation, the patient became more and more drowsy and at times it was difficult to arouse him. There was a rapid decline and death occurred on June 2.

Gross Anatomy.—On reflection of the dura the meninges were found smooth and glistening, and there was no evidence of meningitis. One small area beneath the pia-arachnoid showed evidence of increased intracranial pressure as the gyri were flattened and the sulci were shallow. Over the posterior part of the right frontal lobe there was an oblique incision extending into the depth of the brain. There were two small protrusions at the site of puncture wounds, one anterior to the rolandic fissure and one in the right occipital region. There was no hemorrhage in the cortex.

The body of the right lateral ventricle was almost completely closed for its posterior two-thirds by a growth projecting from its lateral wall (Fig. 27). This growth was rather hard in consistency, rounded and presented posteriorly a cystic and vascular prolongation. Anteriorly this mass presented a raw surface and formed part of a cavity which in its turn formed the mesial termination of the surgical incision into the right lateral ventricle. In front of this mass there was an excavation lined with rough, somewhat necrotic tissue, probably the seat of the neoplasm removed at operation. The operative passage in the right hemisphere was lined by softened, necrotic tissue.

At the base of the brain, the floor of the third ventricle was thinned out and bulging, and the corpora mammillaria were flattened. The cranial nerves were unchanged.

On inspection of the brain a few hours after being placed in liquor formaldehyd, it was noted that in several regions of the cerebral hemispheres there was marked retraction of the gyri, and these on palpation showed great increase in consistency. When such areas were incised, they showed a uniform grayish-white substance with a lack of demarcation between the gray and white matter. Such areas were found in both occipital lobes at their anterior margins, another area in the supramarginal gyri on both sides, and another in the posterior portion of the superior temporal gyrus on the right side. These areas were variable in size, measuring about 1 to 2 square centimeters.

A horizontal incision at the level of the roof of the lateral ventricles brought into view extremely dilated ventricles, the right posterior and descending horns being more distended than the corresponding parts of the opposite side. The ependymal lining of the ventricles was markedly thickened and presented a highly irregular surface with numerous granules and irregularly scattered small papillomatous elevations. This was also seen in the roof of the fourth ventricle (Fig. 28).

Microscopic Anatomy.—Sections of the cerebral hemispheres presented typical areas of tuberous sclerosis showing a loss of normal arrangement of the cortical layers, the presence of primordial elements such as monster giant glia cells and ganglion cells, bipolar ganglion cells; the underlying white matter showed a markedly increased number of glia cells, at times approaching a sclerosis (Fig. 29).

Fig. 27 (Case 14).—Tumor and granular appearance of the ependyma (Tuberous sclerosis).

Fig. 28 (Case 14).—Granulations in ependymal lining of the roof of fourth ventricle (Tuberous sclerosis).

Sections through the tumor mass presented the features of spongioblastoma, with glia cells, giant in size and spindle shape in form (Fig. 30), as the predominating element. The cells were arranged in interlacing bundles. They were spindle shaped, fusiform or occasionally conical in outline, and many of them contained more than one nucleus. The nuclei were rich in chromatic material. Roset formations were also observed (Fig. 31).

CASE 15.—*History.*—I. V., aged 15, admitted to the hospital, Feb. 3, 1919, six months before admission began to suffer with severe frontal headaches,

Fig. 29 (Case 14).—Selected sclerotic area of cerebral cortex, showing monster glia cells, bipolar cells and embryonic ganglion cells.

and these attacks became more and more intense. There were also occasional attacks of vomiting, unrelated to his meals and spells of dizziness and fainting. On consulting a physician, the patient was told that vision in his left eye was impaired, and was causing the headaches. There was no improvement and vision in the left eye failed progressively.

Examination.—On admission the patient was alert. The fundus of the right eye showed papilledema, with a swelling of 1.5 to 2.0 diopters. The veins were very full and tortuous. The left eye showed papilledema in a later stage with incipient pallor of the nerve, but with slight swelling. There was right hemiparesis.

Course.—On Feb. 4, 1919, the patient appeared comfortable on evening rounds, with a fair general condition and pulse slow and regular. About half an hour later, the nurse called a physician stating that the patient was unconscious, the pulse rapid and feeble and the respiration very slow, 4 to 6 per minute. There was salmon red froth oozing from the mouth and nose with each respiration. The corneal reflexes were absent, and the limbs were completely relaxed. The patient died without regaining consciousness.

Gross Anatomy.—The cerebral vessels were markedly engorged at the base of the brain. On the floor of the third ventricle there was a large mass which

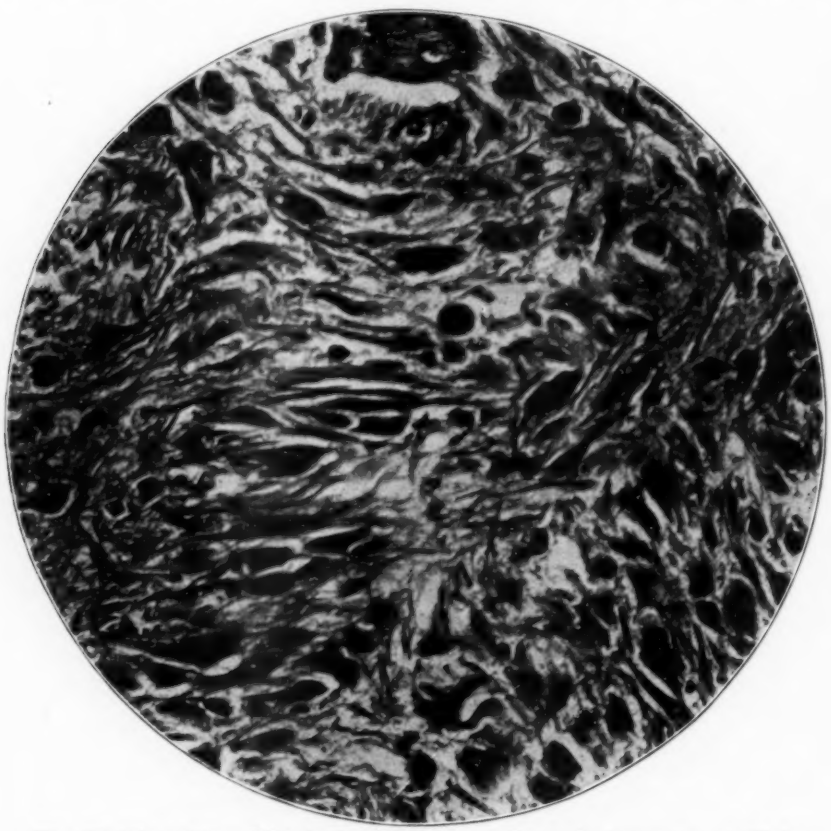


Fig. 30 (Case 14).—Histologic character of the main tumor mass (Tuberosclerosis).

looked like a cyst pressing on the optic chiasm, but on section of the brain this structure was found to be only a part of a large neoplasm, which was embedded in the brain substance in the region of the basal ganglia on the left side and protruded into the third ventricle, completely filling it and closing both foramina Monro (Fig. 32). Both lateral ventricles were markedly distended throughout their extent.

Microscopic Anatomy.—Numerous sections were taken from various parts of the tumor mass, and stained by various methods, but they showed little more than what has been recorded in the preceding cases. Here again giant cells, bearing a strong resemblance to large ganglion cells, formed the predominating

type of cell. They gave off long processes, which, however, failed to react to the Bielschowsky stain (Fig. 33). They arranged themselves about blood vessels or cystlike openings in a radiating fashion, directing their fine filamentous processes to the walls of the enclosures (Fig. 34). In some instances these cellular groupings assumed the form of rosets (Fig. 35). A thorough search of the cerebral cortex resulted in the finding of a number of monster cells, suggesting the picture of an atypical case of tuberous sclerosis.

CASE 16.—*History.*—S. S., aged 47, admitted to the hospital, July 9, 1923, for six weeks had complained of a general feeling of insufficiency. Three days

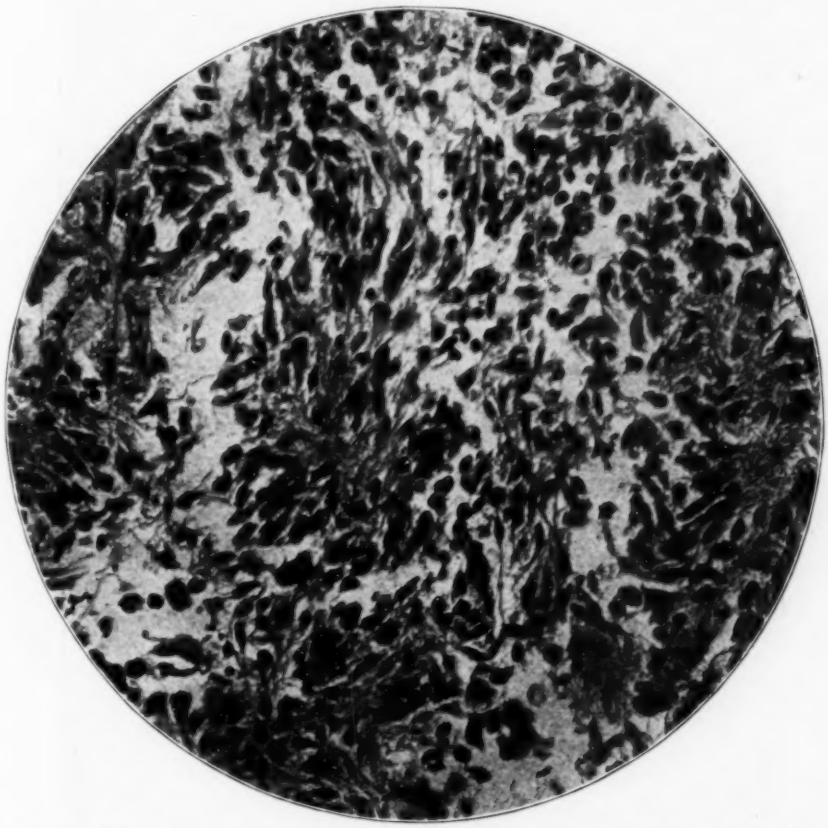


Fig. 31 (Case 14).—Typical area of tumor mass, showing "roset" formations.

before admission he fell to the ground, became very cold and pale, his eyes rolled, and he developed a general muscular spasm, followed by spasticity. The mouth could not be opened and thearms could not be straightened out. He lost consciousness for about ten to fifteen minutes. Three such attacks occurred during the next three days, and they were preceded by the appearance of spots before his eyes. There was no loss of sphincteric control during these attacks.

Examination.—The patient cooperated poorly. He appeared apprehensive and emotionally unstable, showing rapid changes of mood, but mostly of depression. At times he was totally disoriented, at other times totally irrational and at times drowsy with fixed facies. He hiccuped frequently. The

cranial nerves were normal, except the optic, in which the right disk showed slight veiling of the markings on the surface and of its margins. The vessels were normal. The lower half of the left disk was occupied by a congenital crescent; the upper half was blurred by moderate edematous swelling, with vessels increased as they passed from the disk to the retina. The condition was suggestive of a possible developing papilledema. The reflexes were normal; there were no pathologic reflexes and no apparent motor changes. The blood

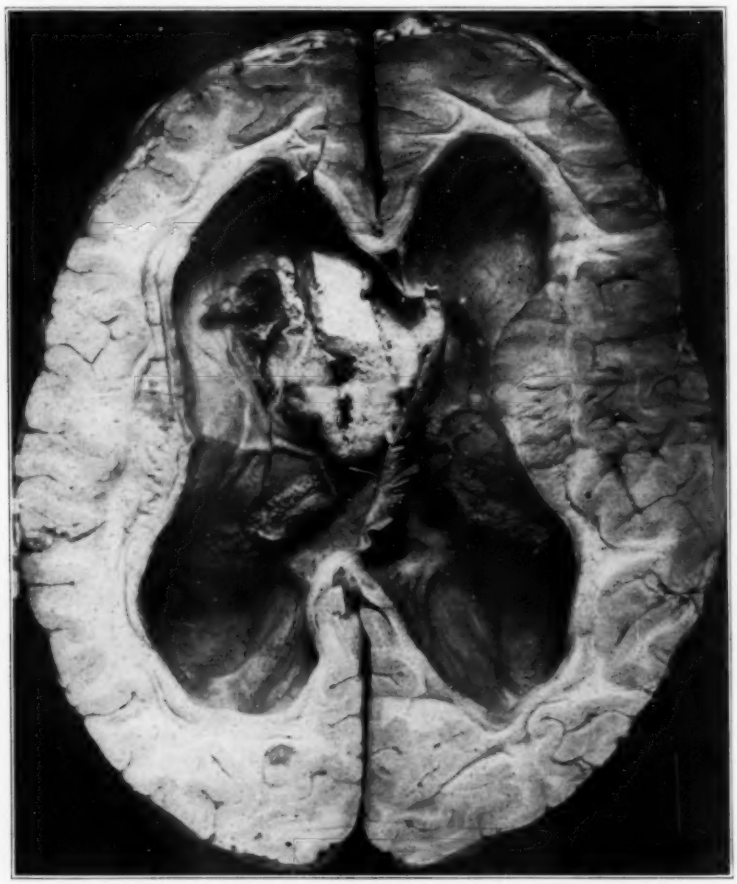


Fig. 32 (Case 15).—Tumor and distention of the lateral ventricles owing to closure of the foramina of Monro by downward growth of the tumor.

pressure was: systolic, 122; diastolic, 84. The cerebrospinal fluid Wassermann test was negative. There were no cells; the globulin test was one plus, and the pressure was normal. Urinalysis was negative, and the blood Wassermann test was negative.

The case was considered to be one of essential epilepsy, in view of the almost negative neurologic status, although roentgen-ray examination showed some calcareous deposits scattered here and there in the skull cavity. The onset of epilepsy so late in life aroused some suspicions.

Course.—The patient was discharged from the hospital at his own request, with the condition unchanged, and readmitted on Jan. 4, 1924. During his stay at home the patient had had several epileptiform attacks. He had spent a week in Bellevue Hospital, where the diagnosis of cerebral neoplasm was considered. One day before readmission he lapsed into semistupor.

Physical examination on readmission showed that the patient was stuporous, and he was aroused with difficulty. The pupils were sluggish to light. There was right facial weakness; and the tongue deviated to the right. The deep reflexes in the upper extremities were active and equal; the abdominal reflexes were diminished, more on the left than on the right. The knee and ankle

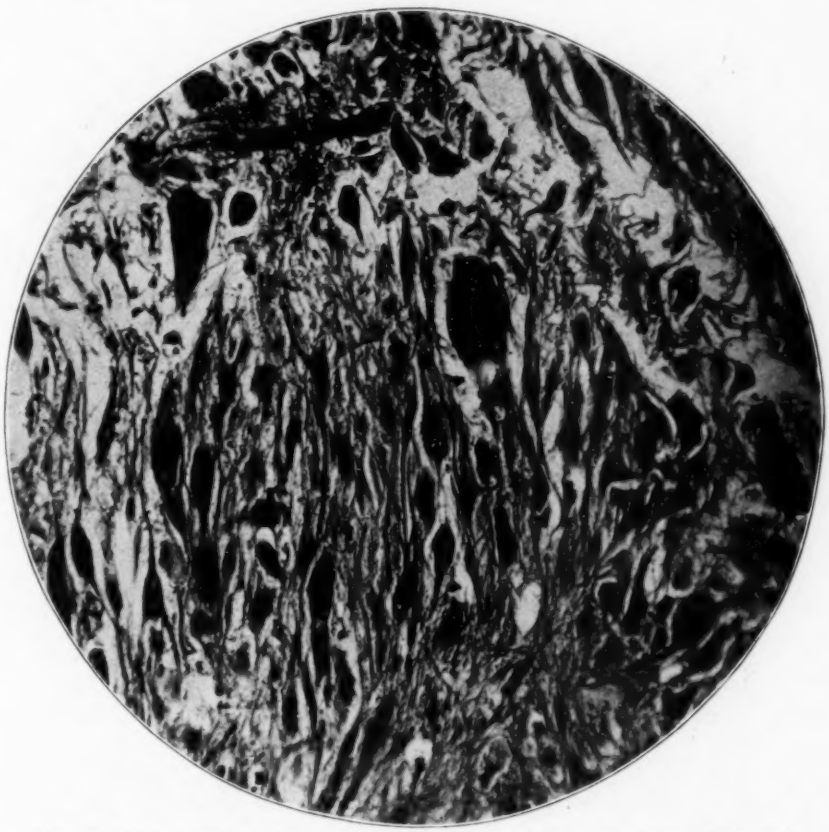


Fig. 33 (Case 15).—Types of cells; monster glia cells (spongioblasts).

reflexes were exaggerated, more on the left than on the right. Ankle clonus was present on the left side, and there was a tendency to clonus on the right. There was a tendency toward a Babinski sign on the left, and there was a questionable plantar reflex on the right. Slight rigidity of the neck was present.

On January 6, the patient was in deep coma, and could not be aroused. The left arm was relaxed; the right arm was stiff and was held in flexion; the hands were relaxed. Both legs were spastic, and a definite Babinski sign was obtained on both sides. There was bilateral clonus, which was more pronounced on the right side.

On January 7, there was left-sided ptosis; the pupils were unequal, the left being larger than the right. There was exhaustible bilateral clonus and right facial weakness (central in type). A few hours later the inequality of the pupils and the ptosis disappeared, but the right facial weakness, the left Babinski sign and the exaggeration of the left deep reflexes and left ankle clonus still remained.

Ventriculography was performed, and the fluid was found to be under increased pressure. A roentgenogram suggested a neoplasm arising from the

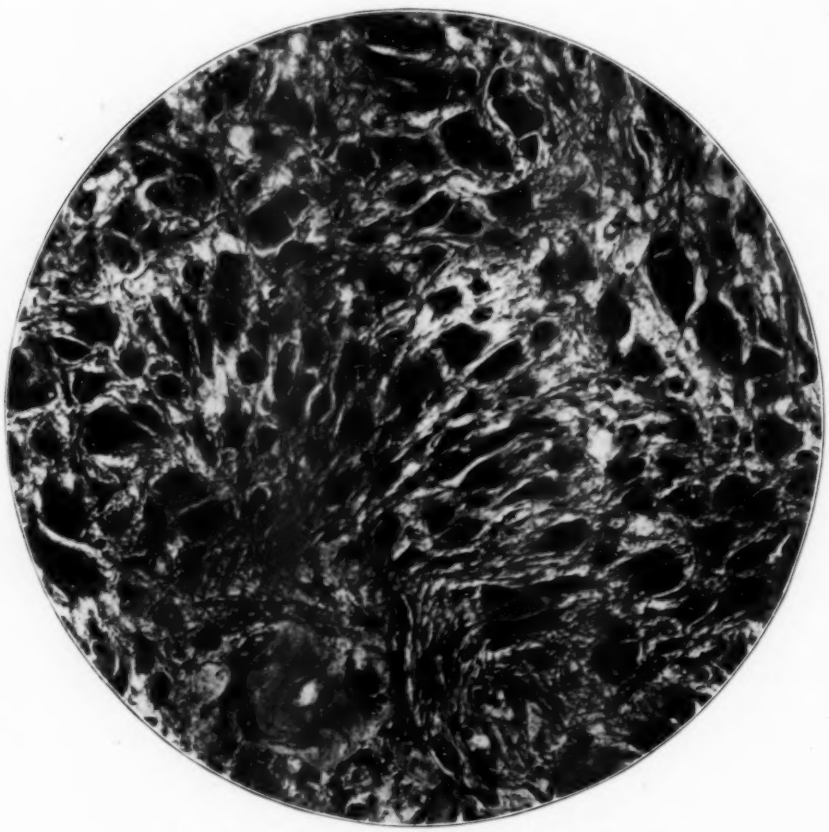


Fig. 34 (Case 15).—Radial arrangement of cells.

orbital surface of the left frontal lobe. The pontile features were interpreted as pressure symptoms.

Craniotomy was performed, but no tumor was noted on thorough exploration of all sides of the frontal, temporal and occipital lobes. A needle was passed in an attempt to locate the growth in the area corresponding to that in which calcareous masses were seen in the roentgenogram, but nothing abnormal was disclosed. It was felt that there was a deep subcortical growth which could not be exposed at operation. The patient died in stupor two days after the operation (Jan. 10).

Gross Anatomy.—The gross appearance was that of a brain with increased intracranial pressure. This was more marked on the left side. The volume

of the brain appeared to be increased, particularly in the region of the left frontal, temporal and parietal lobes. The vessels were congested but showed no atheromatous changes.

Several gyri were more prominent than others. This was true of the post-central gyrus and the middle portion of the middle frontal convolution on the right side. These gyri were increased in consistency, offering more resistance to touch than the rest of the brain. At the base of the brain, the optic chiasm and optic tract showed peculiar swellings. This was particularly true of the right optic tract, which was nodular, swollen and irregular in outline.

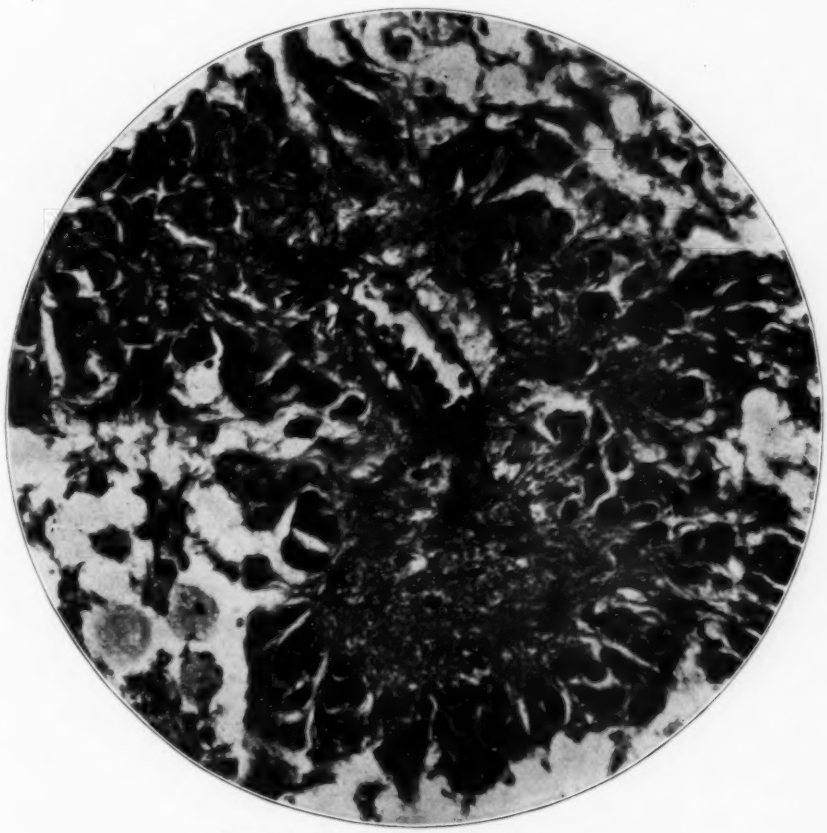


Fig. 35 (Case 15).—Roset formation.

On incision of the brain a large infiltrating tumor was found extending from about 4 cm. posterior to the left frontal pole to the level of the splenium of the corpus callosum. In its course backward, the tumor widened and involved an extensive zone of the left cerebral hemisphere. At the level of the genu of the corpus callosum it extended through that structure and invaded the other hemisphere. At the level of the foramina of Monro the tumor involved almost the entire white substance, invaded the thalamus, a small portion of the internal capsule, and then spread into the temporal lobe, including the hippocampus. Further back, it became still wider in the field of infiltration, and came to a fairly abrupt terminus at the level of the splenium of the corpus

callosum. Throughout its length, the tumor mass presented small nodular structures, which were extremely hard and appeared to be calcified. The ventricles were distorted, the left being compressed dorsoventrally, while the right was somewhat hypertrophied.

Microscopic Anatomy.—Section through the main tumor mass presented a striking picture. About deeply blue stained accumulations of calcareous masses there were fairly wide zones of glial proliferation. The glia cells were of a fusiform type showing an interlacing arrangement, and formed a thick, dense capsule about the calcareous material deposits of which were fairly numerous throughout the preparation. In other places the calcareous deposits

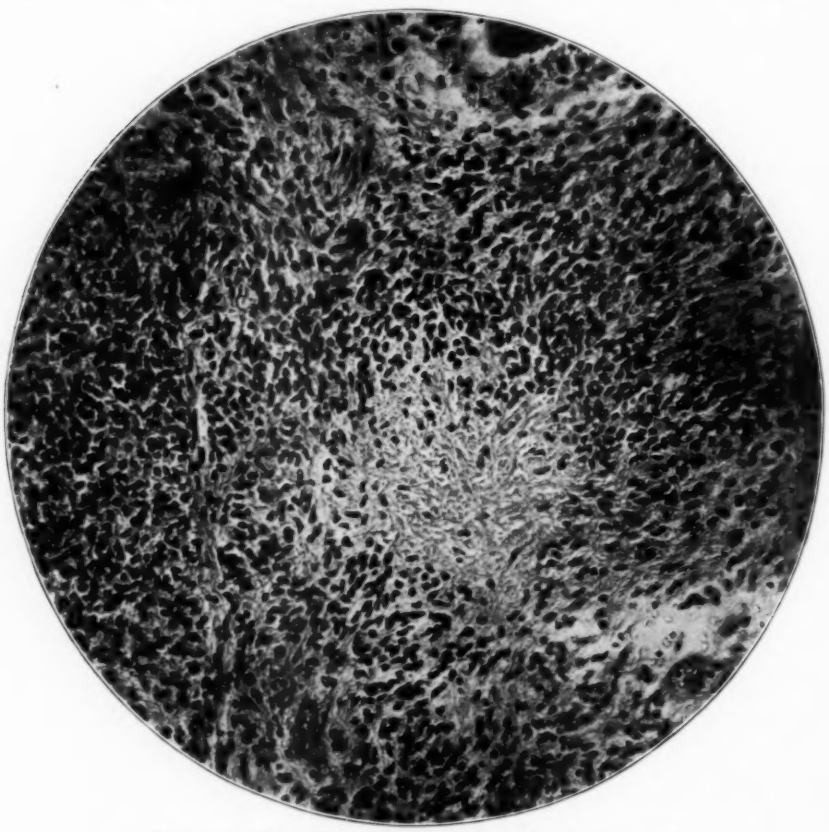


Fig. 36 (Case 16).—Embryonal cell arrangement.

were not encapsulated and rested freely in a mass of loose glial tissue. There the latter assumed alveolar or roset formations (Fig. 36). The periphery of the tumor mass was characterized by loose glia proliferation. There the glial elements gave off fine filamentous processes which anastomosed to form a loose reticulum. In other sections ependymal cysts and productive reactions about blood vessels were seen. In the convolutions which microscopically were characterized by increased consistency and prominence, and which were not involved in tumor growth, there were areas with abnormal ganglion cells of unusually large size and form. In the same areas monster glial cells were also present. The histologic picture was similar to that of tuberous sclerosis of a mild degree.

GENERAL CONSIDERATIONS OF THE ANATOMIC FINDINGS

A summary of the anatomic findings brings forth several gross features, some of which are common for the entire group, while others are to be found only in a certain number of the reported cases. Intense vascularity, markedly destructive properties as shown in extensive necrotic zones, large hemorrhagic foci and cystic degenerative changes are common findings in almost all the tumors described. On the other hand, the appearance of multiple centers of growth at distant points, found in six of our cases, we regard, not as a metastatic phenomenon, but rather, in the sense of Bielschowsky's hypothesis, as an expression of multiple primary centers called into existence by the same cause or causes. It is in this light that the cases of Stroebe, Heubner, Lensden and Schmincke are to be considered, and it would seem that they fit well into our group of spongioblastoma, in which infiltration and multiple foci are rather frequent.

Of course, the mere presence of necrosis, hemorrhage and cystic degeneration does not justify the placing of a glia tumor in the group of the spongioblastoma, but if such features are coupled with typical microscopic findings, and still further amplified by multiple centers of growth, there is little doubt that such a tumor belongs in this group.

By histologic examination we note that the giant cells are common and are apparently a form of unripe and highly atypical spongioblasts. The pyriform cells also play an important part, while other undifferentiated mononuclear elements are much less specific. More striking, however, is the peculiar grouping of the tumor cells.

The radial arrangement of cells about cystlike structures, the roset formations, the alveolar grouping of cells, suggesting a glandular tissue, and the embryonal, palisade order of cells, are all features which may be regarded as typical of spongioblastoma. The absence of extracellular glia fibers, while not a positive identifying feature, is nevertheless of value in distinguishing such tumors from the ordinary gliomas. The cell richness, the proliferative tendencies, the presence of numerous amitotic divisions and occasionally that of mitotic figures are additional evidence of the relative malignancy of such tumors and have justified the term, malignant glioma, a term which we do not consider as appropriate as spongioblastoma.

It will be recalled that earlier in this paper, the spongioblasts and the neuroblasts were considered as cell units representing a similar level of differentiation. This will, no doubt, raise the question, why the spongioblastomas do not follow the course of the neuroblastomas with regard to widespread metastasis. The answer to this question may be found in the fact that neuroblasts are potentially migrating cells, and hence have an inherent property for metastasis, while the migrating

tendency of the spongioblasts is limited in their developmental life by their special morphology. With these differences in mind, it will be understood why some of the primary tumors of the medulla of the suprarenal or other parts of the sympathetic nervous system, which do not display the highly malignant traits of neuroblastoma, are called malignant gliomas. They should be termed spongioblastomas.

It is highly significant that in three cases of our total of 16 we have found pathologic changes characteristic of tuberous sclerosis. These changes varied in degree in the three cases and were found in parts of the brain remote from the seat of the main neoplastic masses. The occurrence of a pathologic process, which is regarded by Bielschowsky as a form of diffuse spongioblastosis, in association with the form of neoplasm which we are describing is suggestive of a closely related etiology.

GENERAL CONSIDERATIONS OF THE CLINICAL FEATURES

A survey of the sixteen clinical records herewith reported shows that almost all of the cases presented an unusual clinical picture for brain tumor. All, but three of them, were characterized by an acute, almost precipitate, onset, an extremely rapid development of the clinical manifestations and an unusually brief clinical course terminating in death. A careful study of the clinical histories of our cases will show that early in their course there was little to suggest the diagnosis of tumor cerebri, and various other diagnostic possibilities were considered.

Our cases have been divided into groups based on the clinical symptoms presented early in the course of the disease. In Cases 1 to 5 and in Case 16 a diffuse inflammatory process such as epidemic encephalitis was seriously considered as the most probable diagnosis. In Cases 6 to 11 a vascular lesion was thought to be the cause of the clinical picture. Cases 12 and 13 were early recognized as cerebral neoplasms. Case 14 presented great difficulty in diagnosis, which is explained by the presence of tuberous sclerosis as well as a tumor.

CONCLUSIONS

1. A glioblastic tumor of the brain and spinal cord is described, for which the name spongioblastoma is suggested. It presents several distinguishing features: (*a*) It is highly cellular. Its cells are embryonal, incompletely differentiated glial elements—the spongioblasts. (*b*) These cells are found in several, transitional forms, such as the giant cell, the pyriform cell and an irregular stellate cell. (*c*) These cells, particularly the giant cells, frequently undergo amitotic division, although mitotic figures are occasionally encountered. They show marked proliferative tendencies. (*d*) The cells, in their grouping, assume various rudimentary formations, alveolar, radial (about cystlike struc-

tures), rosets and palisadal. (*e*) Extensive necrotic zones, numerous hemorrhagic foci and cystic degenerative changes are common. (*f*) Grossly, the tumor can be recognized by its granular appearance, marked vascularity, which gives it a dark, dirty brownish-red hue, by extensive necrotic areas, by marked edema of a wide zone of the neighboring tissue and occasionally by the multiplicity of growth centers.

2. This form of cerebral neoplasm is also characterized by an unusual clinical picture which is marked by acute onset, rapid clinical course and early fatal termination.

3. Because of the atypical clinical features which simulate either an inflammatory or vascular disease of the brain, early diagnosis is exceedingly difficult and often impossible.

4. This form of tumor is occasionally associated with tuberous sclerosis, a form of diffuse spongioblastosis.

5. Such neoplasms are often described under various other names and are frequently called gliosarcoma, a term which is considered incorrect.

MEDULLOBLASTOMA CEREBELLI

A COMMON TYPE OF MIDCEREBELLAR GLIOMA OF CHILDHOOD*

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AND
HARVEY CUSHING, M.D.
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In previous communications from this clinic, it has been pointed out that the true tumors of the central nervous system represent about 40 per cent. of all intracranial neoplasms. Considered as a group, these lesions usually receive the pathologic diagnosis of glioma; this unqualified term implies to many a condition of hopeless malignancy. However, the fact has gradually become appreciated that certain types of glioma are favorable to operative removal and others are favorably influenced by radiation. It consequently is important, more especially for the neurosurgeon, on both prognostic as well as therapeutic grounds, that his clinical experiences should be correlated with a more detailed classification of the gliomas than is customary.

This is a task the authors have set for themselves,[1] and in the course of a preliminary survey of the material at hand, representing the records and tissues of approximately 400 gliomas, we were impressed by the frequency with which there has been encountered (in the large majority of cases in childhood) a very cellular tumor of a peculiar kind, apparently arising over the roof of the fourth ventricle and projecting into the center of the cerebellum.[2]

Accordingly, under the designation of spongioblastoma cerebelli, a series of twenty-five of these tumors was reported at the 1924 meeting of the American Neurological Association. In this terminology we had followed Ribbert,[3] unaware at the time of preparing our paper that

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* From the Surgical Clinic of the Peter Bent Brigham Hospital.

* Presented at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, June 5, 1924.

1. The expenses of these researches have been defrayed by the Philip Gray Fund for the Study of Brain Tumors.

2. Five other tumors unquestionably of the same histogenesis have been encountered among the many gliomas of the cerebral hemispheres. One of these had spread widely through the leptomeningeal spaces forming the picture of the so-called "sarcomatosis of the meninges." The tumors therefore cannot be said to be confined to the region of the fourth ventricle though the percentages show this is by far the more common site, more particularly in children. All four cerebral cases were in adults.

3. Ribbert: Ueber das Spongioblastom und das Gliom, Virchows Arch. f. path. Anat. **225**:195, 1918.

Strauss and Globus had previously and independently of Ribbert employed the identical term.[4]

At the same meeting, Globus and Strauss gave a report on a series of spongioblastomas of the cerebrum, in which the growth shows considerable cellular differentiation not present in the group of cerebellar tumors we had under consideration. It was evident both to these gentlemen and ourselves that it would be unfortunate to confuse the issue by publishing the papers as they stood without modification of the titles; consequently, after interviews with them and a study of their specimens, we shall adopt for our cases the term *Medulloblastoma* as appropriate to the particular tumors to which we independently desire to call attention.

The undifferentiated medulloblastomas to which we shall confine our present discussion have long been recognized as having an unmistakable microscopic appearance which sets them apart from all other tumors of the glioma series. In our Brigham Hospital records, as will be seen, many of them have in the past been designated neurocytomas or neuroblastomas,[5] under what we now believe to be a mistaken conception of their histogenesis. This was partly due to the fact that by the methods of staining for glia in common use the inconspicuous cell processes found in these tumors did not stain like neuroglia, and consequently they were regarded on this negative evidence as probably of neuroblastic origin. However, by the adoption of the more precise methods for staining the processes and fibrils of glia cells introduced by the Spanish school, it has been possible to demonstrate that the cells of these tumors, though in large part undifferentiated, are potential gliocytes rather than neurocytes. This finding serves not only to exclude them from the extremely rare tumors composed in large part of what unquestionably are neuroblasts, but also to exclude them from the group of sarcomas, an equally rare tumor of the nervous system with which they have by many been confused.[6]

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4. Strauss, I., and Globus, J. H.: Spongioblastoma with Unusually Rapid Growth Following Decompression, Neurol. Bull. **1**:273, 1918.

5. These terms were introduced fifteen years ago by J. Homer Wright (J. Exper. Med. **12**:556-561, 1910). All of the twelve tumors which he then reported had presumably originated from the anlage of the abdominal sympathetic system (suprarenal) with the single exception of his Case XI, which proves to be No. 3 of our present series of cerebellar medulloblastomas. The tendency of the cells in the suprarenal tumors toward a roset arrangement, a tendency which is also present in the tumors of the central nervous system under discussion, has been the histologic feature of the lesion on which the diagnosis of neuroblastoma has in large part subsequently been based.

6. Ford, Frank R., and Firor, Warfield M.: Primary "Sarcomatosis" of the Leptomeninges, Bull. Johns Hopkins Hosp. **35**:65-75 (March) 1924.

The tumors, to be sure, are made up of rapidly growing undifferentiated cells resembling those of a round cell sarcoma. But if it can be shown that they are of ectodermal origin and correspond to the undifferentiated cells in the developing cerebellum, their histogenesis is thereby established, and the terminology proposed may well be adopted as appropriate for them.

STAINING METHODS

In order, therefore, to determine whether the cells composing these tumors were of mesodermal or ectodermal origin, and if ectodermal, as was presumed, whether they belonged to the spongioblastic or neuroblastic series, the following methods were employed for displaying the structural characteristics (1) of nervous tissue, (2) of connective tissue, (3) of neuroglia.

If the material had been fixed in Zenker's fluid, it was embedded in paraffin, and the sections were stained with hematoxylin and eosin, Mallory's phosphotungstic acid-hematoxylin, Mallory's anilin blue-orange G, neutral ethyl violet-orange G, and Held's methylene blue-erythrosin. In this way it was possible to identify collagen, reticulum, fibroglial fibrils, neuroglial fibrillae and tigroid substance. There is no way known to us whereby neurofibrillae can be identified in material fixed in Zenker's fluid.

Most of the tissues had been preserved in 10 per cent. formalin, and on this the following methods were employed on frozen sections cut from the same block:

(*a*) For collagen and reticulum, Perdau's method.

(*b*) For neuroglial fibrillae, Hortega's first variant.

(*c*) For protoplasmic glia, Achúcarro's tannic silver method and Hortega's fourth variant.

(*d*) For neurofibrillae, Bielschowsky's method and a recent method of Cajal.

(*e*) For tigroid substance, the method of Bielschowsky-Plein.

For the identification of neurofibrillae, Bielschowsky's method was always used after treatment with pyridin, and even then the sections were always carefully compared with preparations made by the method of Perdrau, for the reticulum of the connective tissue is often sharply impregnated by the method of Bielschowsky. The Bielschowsky preparations were also carefully compared with the Cajal sections.

For the identification of the neuroglia we depended always on Achúcarro's tannic-silver method, which never impregnates nerve fibers. There is no need to compare these with Perdrau preparations, since the intensely black reticulum is easily distinguished from the more delicate neuroglial fibrillae. These fibrillae, as a rule, especially the embryonic ones, are golden brown, though when fully differentiated they may

also appear black. Since these preparations are difficult to photograph, others were made with Hortega's fourth variant at the same time. These have the advantage of lending themselves better to reproduction, but they cannot be relied on to identify neuroglia since axons are impregnated as well.

Achúcarro's method was used in the following way:

(1) Cut frozen sections of formalin-fixed tissue at 10 microns.

(2) Heat to steaming in a 10: 100 solution of pure tannic acid.

(3) Allow to cool. Wash sections in distilled water plus 2 drops of ammonia until they recover their flexibility.

(4) Place in dilute Bielschowsky's ammonia-silver solution (3 or 4 drops to 10 c.c. of distilled water) until the white matter begins to be stained.

(5) Reduce in 20% formalin plus 6-8 drops of ammonia to each 10 c. c.

(6) Wash; dehydrate; clear; mount in balsam.

CASE REPORTS

We are dealing, then, with a well recognized tumor frequently called a neuroblastoma (or when spread through the meninges, a sarcoma), for which we wish to propose a new and more specific term. The tumor is one which may be diagnosed at the bedside with a possible 50 per cent. of accuracy; one which should be capable of type recognition when subsequently exposed at operation; and one for which, when so identified, a generous decompression with subsequent radiation, rather than attempted surgical removal, is the form of treatment to be advocated.

In our original paper prepared a year ago, we had purposely included case reports of the entire series, in order that repetition might serve to emphasize how similar to one another the stories were in all respects—in their clinical history, operative outcome and pathologic findings. This, however, now seems unnecessary, and we consequently have prepared the accompanying table which may give sufficient information for this delayed paper. From the list, which now numbers twenty-nine cases, we have selected for presentation in abstract six examples which will serve to illustrate most of the points we desire to bring out.

The first two cases we present are those in which a fatality occurred without operative intervention. The tissues show the size which the tumor may attain under these circumstances. The pressure effects, both general and local, of a tumor in this situation can be easily surmised. From the first outspoken symptoms, the disease, as will be seen, tends to pursue a rapid course—a matter of a few months.

Cerebellar syndrome with hydrocephalus. Death without operation. Necropsy. Midcerebellar medulloblastoma.

Series of Cases in Which Operation Was Performed

Case	Surg. No.	Sex	Age, Years	Preoperative Symptoms	Operation	Postoperative Survival	Original Diagnosis	Remarks
1	J. H. H. 15498	F	2	9 mo.	Dec. 17, 1903, radical extirpation	4 mo.	Sarcoma	
2	J. H. H. 16736	M	7	5 mo.	Sept. 26, 1904, suboccipital decompression	4 mo.	Gliosarcoma	
3	J. H. H. 24398	F	9	6 mo.	June 13, 1909, partial extirpation	Fatality	Neuroblastoma	
4	J. H. H. 24714	M	6	5 mo.	1. Oct. 5, 1909, suboccipital decompression 2. Oct. 13, 1909, attempted extirpation	Fatality	Neuroblastoma	
5	J. H. H. 25600	M	7	3 mo.	1. March 21, 1910, suboccipital decompression 2. July 19, 1910, attempted extirpation	4 mo. Fatality	Sarcoma	
6	P. B. B. H. 29	M	28	3 mo.	1. March 3, 1913, suboccipital decompression 2. Sept. 15, 1913, partial extirpation 3. June 3, 1914, radical extirpation	21 mo.	Glioma	
7	P. B. B. H. 320	F	6	5 mo.	None; sudden death	.....	Neuroblastoma	
8	P. B. B. H. 1976	F	5	3 yr.?	Oct. 29, 1914, partial removal	3 mo.	Glioma	
9	P. B. B. H. 2175	M	8	4 mo.	Dec. 14, 1914, partial extirpation	2 mo.	Glioma	
10	P. B. B. H. 2527	M	15	2 mo.	None; sudden death	.....	Glioma	
11	P. B. B. H. 2864	M	15	3 mo.	1. May 8, 1915, suboccipital decompression 2. Jan. 21, 1916, radical extirpation	9 mo.	Glioma	
12	P. B. B. H. 3442	M	6	2 mo.	1. Aug. 26, 1915, partial extirpation 2. May 31, 1916, extirpation	10 mo. Fatality	Glioma	
13	P. B. B. H. 5611	M	10	2 mo.	Nov. 3, 1916, suboccipital decompression	16 mo.	Glioma	
14	P. B. B. H. 11606	M	6	9 mo.	Dec. 8, 1919, suboccipital decompression	21 mo.	Neuroblastoma	Series of radium treatments
15	P. B. B. H. 11785	F	27	15 mo.	Jan. 10, 1920, partial extirpation	23 mo.	Neuroblastoma	Two roentgen-ray treatments, with great improvement; spinal metastasis
16	P. B. B. H. 12416	F	3	10 mo.	May 21, 1920, partial extirpation	4 mo.	Glioma	Four roentgen-ray treatments unavailing improvement
17	P. B. B. H. 13981	M	6	7 mo.	Feb. 14, 1921, partial extirpation; removal of arch of atlas	Living	Neurocytoma	Five roentgen-ray treatments; relief for 48 months
18	P. B. B. H. 15555	M	28	2 mo.	Nov. 21, 1921, partial extirpation	Fatality	Neuroblastoma	
19	P. B. B. H. 16059	F	10	2½ mo.	1. Feb. 13, 1922, cyst evacuated 2. May 27, 1922, tumor extirpated	22 mo.	Glioma	Data concerning treatments unavailable
20	P. B. B. H. 17428	M	5	1½ mo.	1. Sept. 30, 1922, suboccipital decompression 2. March 25, 1924, laminectomy	21 mo.	Glioma	Active roentgen-ray treatment; developed spinal metastasis; no return of cerebellar symptoms
21	P. B. B. H. 18793	F	2	3 mo.	May 16, 1923, partial enucleation	12 mo.	Glioma	Three roentgen-ray treatments
22	P. B. B. H. 18901	F	12	12 mo.	1. June 18, 1923, suboccipital decompression 2. June 27, 1924, radical extirpation	12 mo. Fatality	Neurocytoma	Six roentgen-ray treatments
23	P. B. B. H. 19386	M	21	2 mo.	Aug. 22, 1923, partial extirpation	9 mo.	Glioma	Five roentgen-ray treatments; no return of cerebellar symptoms; death from spinal metastasis
24	P. B. B. H. 19775	F	9	3 mo.	Oct. 1, 1923, partial extirpation	3 mo.	Glioma	Two roentgen-ray treatments with temporary improvement; treatments not pursued
25	P. B. B. H. 21199	M	13	8 mo.	May 1, 1924, suboccipital decompression	6 mo.	Spongioblastoma	One roentgen-ray treatment
26	P. B. B. H. 21341	M	22	16 days	May 23, 1924, subtemporal decompression	Fatality	Neurocytoma	Acute onset following trauma; tumor an unexpected necropsy finding
27	P. B. B. H. 22167	M	6	3 yr.? 2 mo. rapid	Sept. 17, 1924, partial extirpation	Living	Glioma	Eight roentgen-ray treatments
28	P. B. B. H. 22601	M	9	24 mo.?	Nov. 25, 1924, fragmentary extirpation; removal of arch of atlas	Living	Glioma	One roentgen-ray treatment at P. B. B. Hospital; others elsewhere, number unknown
29	P. B. B. H. 22773	M	6	2 mo.	Dec. 11, 1924, extensive extirpation	Fatality	Neurocytoma	Tumor disclosed by incision of vermis

CASE 7.—*History.*—On Aug. 13, 1913, Mary M., aged 6½ years, a school girl, referred by Dr. William Sheehan of Salem, was admitted to the hospital, complaining of headache, vomiting, impaired vision and staggering gait. She had been a healthy child until the onset of her present symptoms, which were of only four months' duration. They were inaugurated by pressure symptoms, i.e., by severe headaches and attacks of vomiting. For two months there had been marked static instability with staggering. Her vision had been failing rapidly.

Examination.—This showed an emaciated, fretful and somewhat disoriented child with an enlarged head due to separation of the sutures. There was a bilateral choked disk with hemorrhages, a bilateral abducens palsy and no nystagmus. She was unable to walk without support. A marked incoordination of cerebellar type affected all extremities.

Course of Illness.—She became worse rapidly, and a few days after admission had a series of convulsive seizures of cerebellar type. These were accompanied by unconsciousness with marked retraction of the head and extensor rigidity of the extremities. In one of these attacks respiration ceased, and although artificial respiration was given until the ventricle could be punctured, the child did not recover. Permission was given for an examination of the brain, which was removed shortly after death. Complete necropsy was not performed.

Pathological Findings.—The brain was fixed with formalin before removal. It showed a marked hydrocephalus and a full cerebellum with a smooth midline tumor presenting between the herniated tonsils of the hemispheres (Fig. 1). A sagittal section (Fig. 2) disclosed a fairly well circumcised, median, spherical cerebellar tumor, overlying the fourth ventricle but not attached to it. The tumor gave the appearance of possibly arising from the tela choroidea. It blocked the iter, which was dilated to the size of a lead pencil.

Histologically the tumor was composed of an irregular mass of rounded cells (Fig. 3), with scanty cytoplasm and oval nuclei containing an abundant reticulum of chromatin. Intercellular fibrillar material was abundant. It contained a scanty reticulum of connective tissue and a few well developed neuroglia fibrillae, but consisted for the most part of numerous embryonic glia fibrillae (Fig. 4). These embryonic fibrillae stained with neither phosphotungstic acid hematoxylin, neutral ethyl violet orange G, nor Hortega's first variant, but were easily impregnated by the fourth variant. The centrosomes usually occurred as a single heavy granule, although diplosomes and rarely a triplosome were seen. No neurofibrillae could be found.

Comment.—The rather sudden, stormy onset of general pressure symptoms shown by this child is typical of most of the other cases in the series. The headache, vomiting and choked disk usually precede the signs indicating the location of the lesion. Indeed, the usual cerebellar tumor syndrome may be incomplete through the absence of a definite, sustained nystagmus. The inaugural pressure symptoms are unquestionably due to cerebrospinal fluid stasis, an inevitable and early complication of a tumor arising from the roof of the fourth ventricle. As the hydrocephalus forms, the cranial sutures may separate and more or less relieve the pressure symptoms, though rarely, even in young children, before the optic nerves have been seriously damaged.

The tissues in this case had been carefully studied by Professor Councilman, then pathologist to the hospital. The tumor was at first regarded as a neuroblastoma, but on further study, which revealed the presence of a few adult neuroglia fibrils which stained with phosphotungstic acid hematoxylin, the diagnosis was changed to glioma.

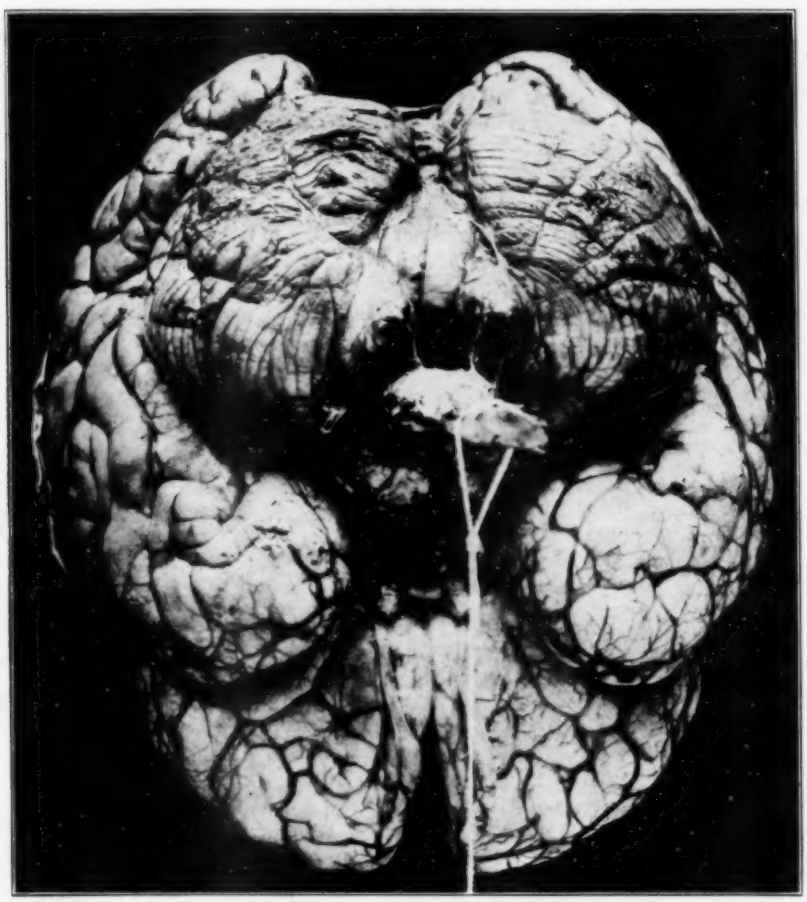

Fig. 1 (Case 7).—Mesial tumor presenting between cerebellar tonsils with brain stem being pulled away.

In the following case the symptoms were still more abrupt in their appearance. Scarcely eight weeks elapsed from the time of their onset to the child's death.

Rapid onset of cerebellar symptoms with hydrocephalus. Sudden death from respiratory failure. No operation. Necropsy. Midcerebellar medulloblastoma.

Case 10.—*History.*—On Feb. 22, 1915, Russel S., aged 15 years, a schoolboy, referred by Dr. J. H. Pratt, was admitted to the hospital, complaining of head-

Fig. 2. (Case 7).—A sagittal section of the hind brain, showing the centrally situated lesion which has flattened the brain stem and widened the ventricle.

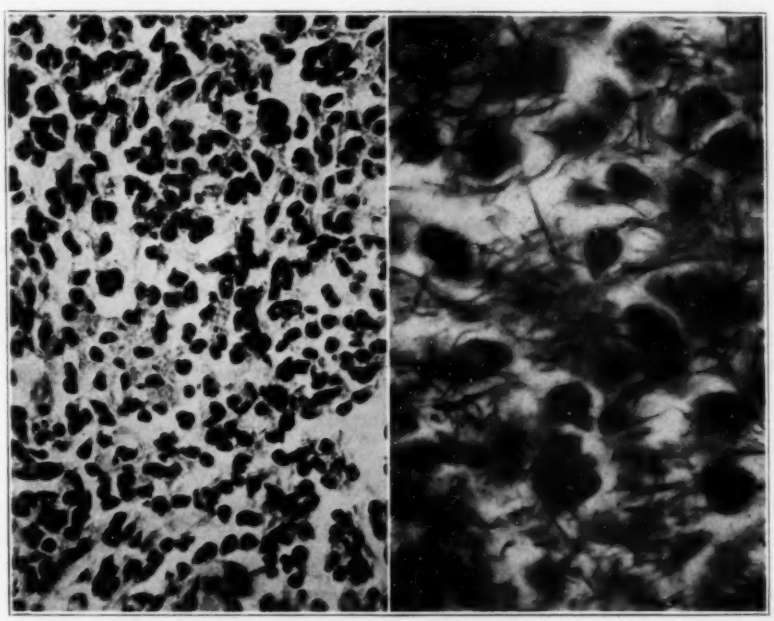

Fig. 3 (Case 7).—Structureless arrangement of cells; iron hematoxylin stain; × 300.

Fig. 4 (Case 7).—Processes of embryonic glia which do not stain with phosphotungstic acid hematoxylin; Hortega's fourth variant; × 850.

ache, vomiting, failing vision and staggering gait. The patient was said to have been in perfect health until Christmas, 1914, when he first complained of double vision and unsteadiness. Early in January he began to have periodic frontal headaches, which have persisted and which have usually been accompanied by vomiting. Since February 1 his vision had been failing, and his speech had been indistinct.

Examination.—This showed an emaciated boy who held his neck stiffly, with the head tilted to the right. There was a bilateral choked disk, with elevation of 8 diopters and extensive retinal hemorrhages. There was also paresis of the left abducens, nystagmus on looking to the right and left, dysarthria, and marked incoordination of cerebellar type of all the extremities. He was unable to stand unsupported.

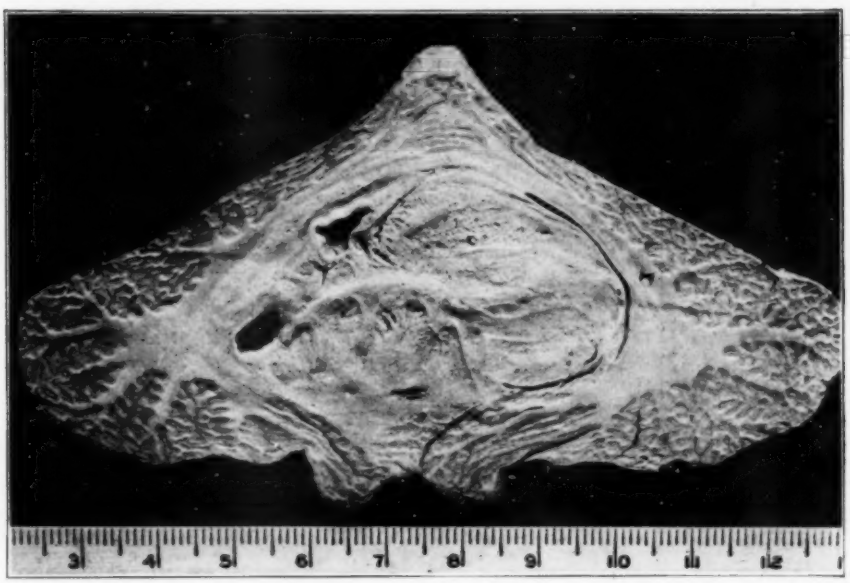

Fig. 5 (Case 10).—Cross section of cerebellum to show centrally placed tumor.

Course of Illness.—On the morning of Feb. 25, 1915, when about to be given an enema as part of his preparation for operation, he suddenly ceased breathing and died in a short time, in spite of artificial respiration. A complete necropsy was performed four and one-half hours postmortem.

Necropsy Findings.—No abnormalities were found elsewhere than in the brain. This had been fixed in 10 per cent. formalin. In addition to marked internal hydrocephalus, a fairly well circumscribed, midcerebellar tumor was disclosed (Fig. 5). At its periphery were two small cysts.

The tumor was studied and described in detail by Dr. Councilman, who pointed out among other things that the microscopic examination showed the tumor to be invading the cerebellar cortex; that islands of tumor cells were found far out in the molecular layer; and that at one place they appeared actually to be invading the leptomeninges. He observed that the general mass of the tumor consisted of closely packed, rounded or pear-shaped cells of

small size with oval nuclei containing a heavy reticulum of chromatin (Fig. 6); that mitotic division of the nuclei was common and that amitotic division was also present. Occasional neuroglia fibers were demonstrated by Mallory's stain, and a diagnosis of glioma of the cerebellum was made.

In addition, it is possible today to show that the intercellular material consists almost entirely of the processes of the neoplastic cells which are unipolar spongioblasts in various stages of formation (Fig. 7). The centrosome occurs as a single granule at the base of the protoplasmic process (Fig. 27). Occasionally adult neuroglia fibrillae can be differentiated in these processes. Here and there are necrotic areas around which the cells are collected in such a way as to form the sort of pseudo-epithelium which has been described by Saxer.

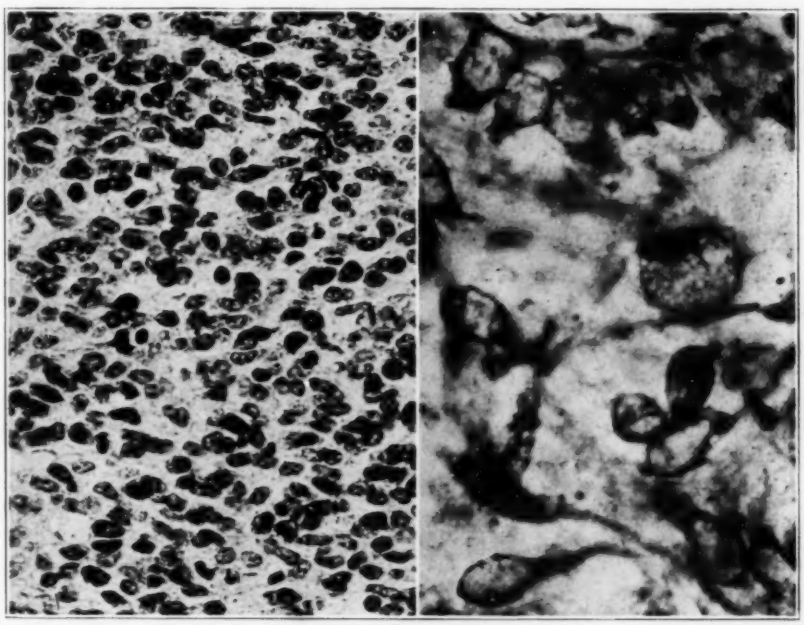

Fig. 6 (Case 10).—Structureless arrangement of tumor cells. Hematoxylin eosin stain; × 300.

Fig. 7 (Case 10).—Note shape of cells, particularly the pear-shaped cell with long process. Perdrau's method modified; × 850.

Comment.—A sagittal section through the cerebellum showed that the lesion occupied exactly the same midline relation to the fourth ventricle as shown in Figure 1. It had no attachment to the floor of the ventricle but appeared to lie above the tela; it extended upward as a roundish ball about 5 cm. in diameter; it occluded the iter which was greatly dilated. It is impossible of course to tell how long the tumor may have existed as a quiescent lesion; but this probably was not long, for an obstructive hydrocephalus was inevitable, and full-blown pressure symptoms must have followed quickly. As these tumors are likely to

project into and occlude the foramen magnum, a lumbar puncture under these circumstances is particularly dangerous. Opisthotenoid seizures with respiratory embarrassment or failure are the usual terminal clinical features of such a lesion.

The remaining twenty-seven patients with tumors in the series have all been subjected to operation, in some instances to successive operations, in what now appears to have been the vain hope that they might be enucleated. The temptation is great, for at first sight the lesion appears to be well encapsulated, and the cerebellum can be readily brushed away from its surface. The tumors, moreover, are fairly tough and can be handled easily, and, as stated above, they involve the roof only and not the floor of the ventricle.

In these twenty-seven cases there have been thirty-six operations, with eight postoperative fatalities, two of them after secondary operations. This gives a high mortality, though one which is perhaps not exceptionally so when one considers the situation of the lesion, the fact that the operation often necessitates the removal of the laminae of the atlas, and the fact that unless the procedure serves to reestablish the cerebrospinal circulation a bad matter may be made worse by the decompression.

The next case is an example of an operative fatality following the attempted removal of one of these tumors.

A six months' history of a midcerebellar tumor. Partial extirpation. Postoperative fatality. Necropsy. Medulloblastoma.

CASE 3.—*History.*—On July 9, 1909, Blanche R., aged 9, a schoolgirl, was admitted to the Johns Hopkins Hospital, complaining of headaches, vomiting and instability. A normal, bright child, she had enjoyed almost perfect health until her present illness. This began in January, 1909, when she complained of occasional frontal headaches, and it was noticed that she was unsteady on her feet and had a habit of rolling her head backward. The headaches soon became associated with spells of vomiting. These symptoms increased progressively in severity until by April she was unable to walk alone, and her vision had become impaired. At about the same time an internal squint of the right eye was noticed, and a few weeks ago of the left, together with a facial weakness on the same side. She had also had tinnitus in the left ear.

Examination.—On admission she had a bilateral choked disk progressing to atrophy, a cracked-pot sound on percussion of the skull, with separation of the sutures, a bilateral abducens palsy, and paresis of the left facial nerve (Fig. 8). In addition there was marked incoordination of cerebellar type of all four extremities; she was unable to stand or walk alone.

Course of Illness.—At operation, on June 13, 1909, a suboccipital exploration revealed a large solid reddish tumor in the center of the cerebellum. A mass the size of a pigeon's egg was enucleated, leaving a raw, blood stained pocket. The child endured operation poorly, and died three hours later. Necropsy was restricted to an examination of the brain, which was removed after formalin fixation in situ.

Pathology.—A block of the tumor which had been removed at operation and immediately fixed in Zenker's fluid was forwarded to Dr. Mallory for a histologic report. Recognizing its resemblance to the tumors which Dr. Homer Wright was then studying, the case was included as Case 12 in Dr. Wright's series of neuroblastomas, with the bare statement that "the tumor shows the characteristic ball-like arrangement of cells and fibrils." No other histologic study of this tumor seems to have been made (Fig. 9).

The Zenker-fixed specimen removed at operation is available for examination, and the brain and the remnant of tumor which showed on coronal section (Fig. 10), as a discrete, rounded, centrally placed mass, 4.5 x 3 cm., overlying the fourth ventricle, together with some clotted blood.

Fig. 8 (Case 3).—Left facial and abducens palsies.

A restudy of the tumor showed it to be composed of a mass of cells without any particularly distinctive architectural arrangement (Fig. 11). The nuclei were round or oval, with an abundant network of chromatin. Cytoplasm was scanty. No centrosomes were seen. Occasional mitotic figures were found. Blood vessels were large but not very numerous. There was a small amount of intercellular fibrillar material, consisting of reticulum, embryonic glia (Fig. 12) and some well developed neuroglia fibrillae. Collagen was restricted to the walls of the blood vessels. Even in the formalin-fixed material no neurofibrillae could be demonstrated.

This case has obscurely found its way into the literature not only in connection with Dr. Wright's report, but also in regard to another matter once made the subject of study by the senior author: namely,

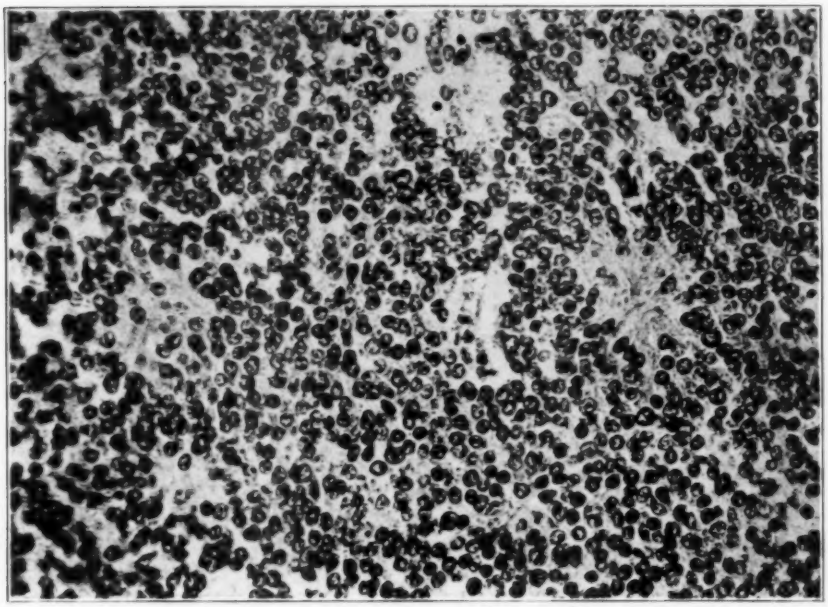

Fig. 9 (Case 3).—Ball-like arrangement of cells. Phosphotungstic acid hematoxylin stain; × 300.

Fig. 10 (Case 3).—Centrally situated tumor.

in connection with internal squint as a false localizing sign of tumor.[7] This case happened to be one of those which was reported at that time as an example of strangulation of the abducentes (Fig. 13). As a matter of fact, an abducens palsy, often bilateral, is of common occurrence in many cerebellar tumors, possibly more common, it would appear, in these midline tumors than in any others. Indeed, it is the one outstanding symptom in addition to the general pressure symptoms brought about by the hydrocephalus and the instability and cerebellar ataxia which the patients show. Whether the squint is actually due to such

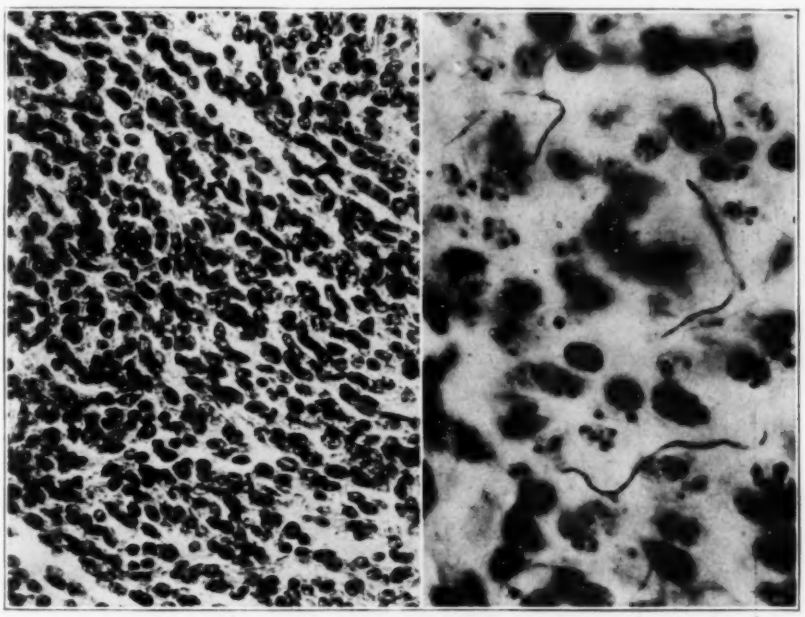

Fig. 11 (Case 3).—General appearance of the tumor on section. Hematoxylin eosin stain; × 300.

Fig. 12 (Case 3).—Processes of embryonic glia demonstrated by Hortega's fourth variant; × 850.

a mechanical cause cannot be definitely asserted. The fact that in this child there was a facial palsy on one side would perhaps be a further argument in favor of the direct implication by pressure of the nuclei for the sixth and seventh nerves.

In the series of twenty-nine cases, there has been only one in which a widespread "sarcomatosis" of the meninges has been observed. The

7. Cushing, H.: Strangulation of the Nervi Abducentes by Lateral Branches of the Basilar Artery in Cases of Brain Tumor, Brain **33**:204-235 (Oct.) 1910.

case happens to be another of those in the Baltimore records of the senior author. It is as follows:

Median cerebellar medulloblastoma with wide dissemination in the leptomeningeal spaces. Original pathologic diagnosis, meningeal sarcoma. Fatality at second operation. Necropsy.

CASE 5.—*History.*—On March 16, 1910, George B., aged 7, a schoolboy, was admitted to the Johns Hopkins Hospital, complaining of headache, double vision, vomiting and unsteady gait. He had been in good health until early in January, 1910, when he had his first symptoms of suboccipital pain and vomiting. By February, double vision was noted. He rapidly became worse. For the past month his gait had been unsteady, and he had vomited frequently. Three

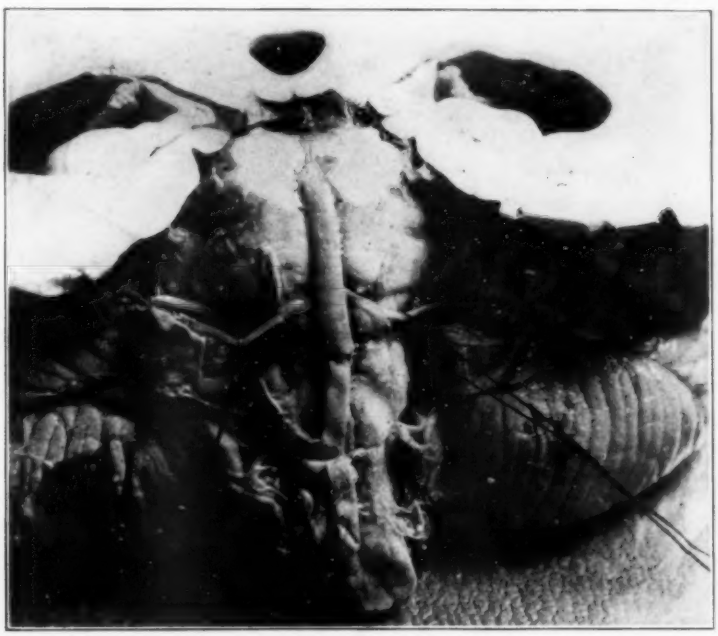

Fig. 13 (Case 3).—Strangulation of the abducens produced by lateral branches (drawn away by threads) of the basilar artery.

weeks prior to admission, he had an "attack" characterized by retraction of the head, Cheyne-Stokes respiration and unconsciousness which lasted for three days. Tuberculous meningitis was suspected. A similar attack occurred a few days before his entrance to the hospital.

Examination.—On admission he was stuporous and his head was retracted. Percussion of the skull gave a cracked pot sound; the eyes showed a bilateral choked disk with elevation of 7 diopters. There was a definite Kernig sign; knee reflexes were not obtainable; gait and station were impossible to test; there was no nystagmus.

Course of Illness.—A bilateral cerebellar exploration was performed on March 21, 1910. An extremely tense cerebellum was exposed, on the surface of which were two discrete nodules of a soft, grayish tumor. One was removed

for study. It was necessary to puncture the lateral ventricle to diminish tension sufficiently to close the wound. On examination the tissue showed what was taken to be an invasion of the meninges by a small round cell sarcoma.

The child made a temporary marked improvement and was discharged. He continued to do fairly well until July when he had a severe cerebellar "fit" similar to those preceding his first operation, and he was brought back to the hospital for observation. An operation seemed to offer the only hope of giving further relief. On July 19, 1910, a reexploration was made of the cerebellar region, with partial extirpation of a lobular, soft, apparently encapsulated tumor

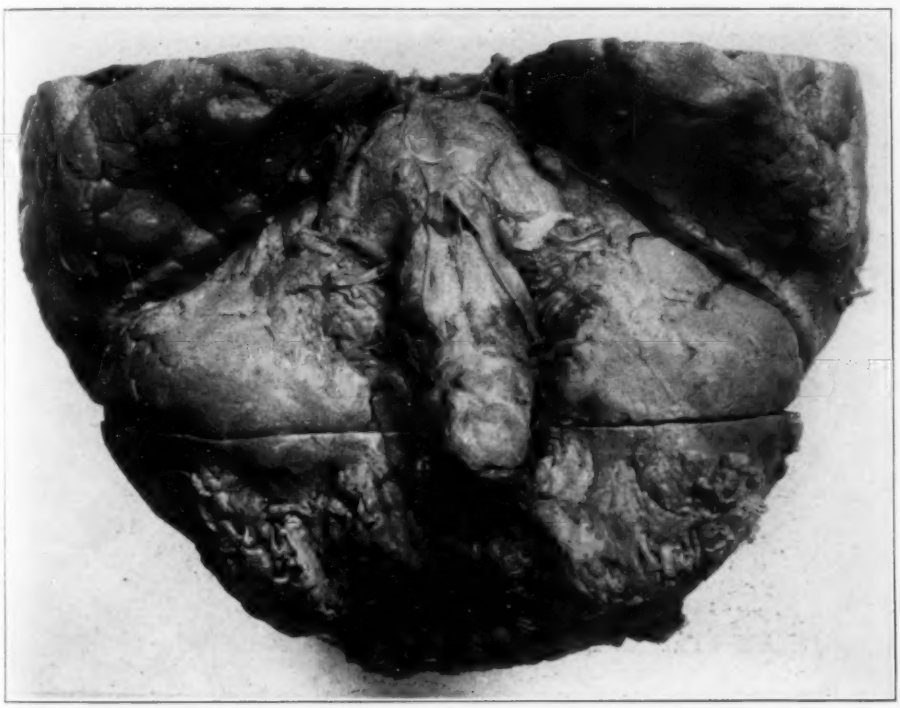

Fig. 14 (Case 5).—Tumor extension throughout the cerebellar leptomeninges.

from the center of the cerebellum. The tumor proved to be of great size, and several large masses of it were removed. The child died not long after the termination of the operation.

Necropsy Findings.—The postmortem examination was limited to the examination of the brain which was fixed by formalin injection before removal. It showed a marked hydrocephalus. It was evident that the intracerebellar portion of the tumor had been almost completely removed, but the growth has spread in the meningeal spaces solidly over the cerebellum (Fig. 14), and in patches over the cerebral hemispheres, where it was visible as flat nodules in the sulci under the arachnoid membrane (Fig. 15). The spinal cord was not examined.

There was available for reexamination some of the material removed at operation and fixed in Zenker's fluid, and the brain fixed in 10 per cent. formalin. The cerebellar tumor was composed of an irregular mass of cells with oval nuclei containing an abundant reticulum of chromatin (Fig. 16). The cytoplasm of these cells was fairly abundant, and there was a large amount of intercellular fibrillar material, consisting of reticulum, collagen, protoplasmic processes of the cells, and numerous adult neuroglia fibrillae which stained with phosphotungstic acid hematoxylin (Fig. 17).

In the nodules of tumor over the surface of the brain the cells were almost similar, but there were more collagen fibers and no neuroglia fibrillae. Mitotic figures were common.

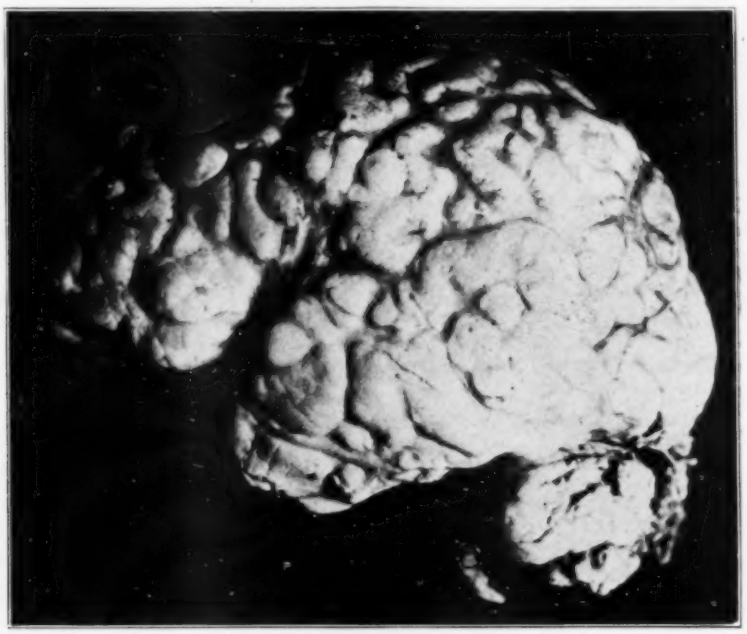

Fig. 15 (Case 5).—Nodules of tumor through the leptomeningeal spaces over the cerebrum.

The midcerebellar tumor in this case was of precisely the same character as that in all the others, but it must be admitted that the meningeal nodules, examined alone, might easily give the impression of a sarcomatous invasion. If we had known as much as we do today about these conditions, it is improbable that this child would have been subjected to his secondary and what proved to be his fatal operation. But there can be no doubt of the marked temporary improvement for three or four months after the first operation, which amounted to nothing more than a decompression.

Attention may be called to the fact that the meninges in this case were found to be "infected" by the tumor when the cerebellum was

first exposed, so that the spread of the lesion into the leptomeningeal spaces was not due to the operation. As a matter of fact, such an occurrence seems to be less common than one might expect in consideration of the active cell division which characterizes these lesions. Of the twenty-nine cases, excluding this particular one, there have been only three in which it was assumed that the spinal meninges had become "infected" by a tumor implant; and in one of them such a metastasis was verified by a laminectomy performed elsewhere.[8]

We have so far cited two examples of the tumors in question which proved fatal without operative intervention; a case in which operative

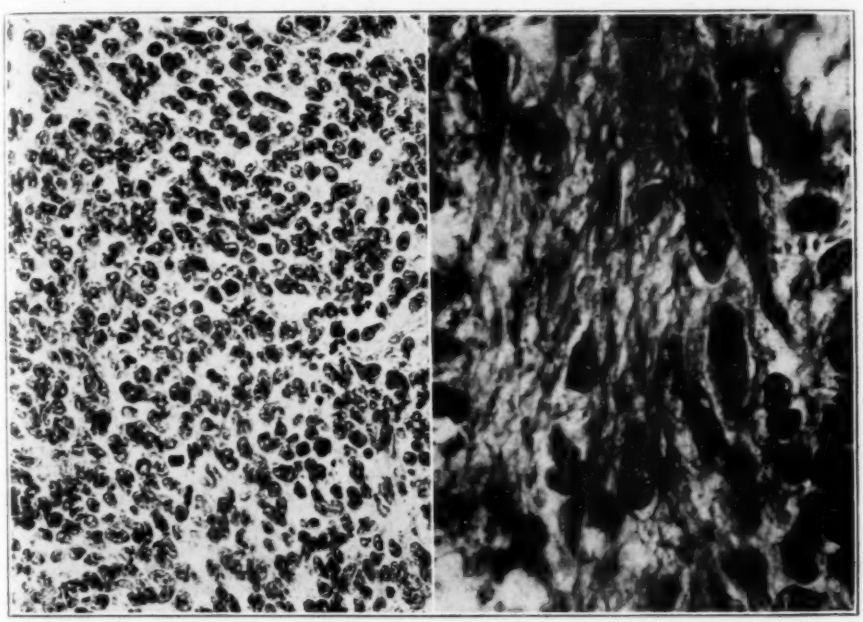

Fig. 16 (Case 5).—Usual structureless arrangement of cells. Phosphotungstic acid hematoxylin stain; × 850.

Fig. 17 (Case 5).—Adult neuroglial fibrillae which stain with phosphotungstic acid hematoxylin; × 850.

intervention led to a fatality, and a case which was characterized by the invasion of the meninges by the tumor. The following case will show that the survival period after adequate decompression and partial enucleation of the tumor with immediate recovery from the operation may nevertheless be brief. The story is of less interest from a clinical than from a pathologic standpoint. Though an early case in the series, the operative tissues happened to have been fixed in formalin, and the

8. Elsberg, Charles A.: Tumors of the Spinal Cord, New York, Paul Hoeber, 1925, p. 161, Case LIV.

tumor proved to be one in which there was a larger amount of the internuclear fibrillar material than usual. It is chiefly for this reason that the case has been selected for report.

Characteristic symptoms of five months' duration. Temporary improvement following partial extirpation of tumor. Death two months later. No necropsy.

Case 9.—*History.*—On Dec. 6, 1914, Louis E., a schoolboy, aged 8 years, referred by Dr. E. H. Beall of Fort Worth, Texas, was admitted with the complaint of headache, vomiting, unsteadiness and incontinence. With the exception of occasional slight headaches, he had always been well until July, 1914, when his major symptoms appeared with the usual abruptness—frontal headache, projectile vomiting, unsteadiness, dizziness and diplopia. These symptoms gradually increased in severity. He was given a course of antisyphilitic treatment, with apparent improvement. In September, it was first noticed that he had some incoordination of his upper extremities. In November, slight nystagmus and optic neuritis were first observed. For the past two weeks, he had been incontinent of urine.

Examination.—On admission, he had wide pupils, a bilateral choked disk advancing to atrophy, nystagmus on looking to the right and left, a divergent strabismus, dysarthria, incoordination of all the extremities of cerebellar type, more marked on the left side. He was too ill to test gait and station.

Course of Illness.—On Dec. 14, 1914, at operation the usual bilateral suboccipital exposure, after ventricular puncture, revealed a full cerebellum with marked foraminal herniation but no evidence of tumor. A transverse incision through the left hemisphere came down on a firm, dark red tumor situated in the middle of the cerebellum. Though vascular, it was apparently encapsulated and thought to be enucleable. A mass about the size of a bantam's egg was extirpated. The child made an excellent recovery from this operation, with relief from headache and vomiting, subsidence of choked disk and improvement in ataxia, so that he was able to walk about with slight assistance. He was discharged, Jan. 7, 1915. The improvement was brief. A month after his return home he became worse again, had respiratory and deglutitory difficulties and died on Feb. 21, 1915. No postmortem examination was made.

Pathologic Examination.—The material removed at operation was fixed immediately in 10 per cent. formalin. Dr. Councilman, though recognizing the resemblance of the tumor to the preceding examples in the series, called special attention to the similarity with another fourth ventricle tumor which proved to be an ependymoma. The demonstration of occasional adult glia fibrils caused him to place the tumor in the glioma group.

As in the other cases in the series, the tumor was composed of an irregular mass of cells (Fig. 18), with rather numerous, thin-walled blood vessels. There was perhaps a greater abundance of intercellular fibrillar material than usual; it consisted of some connective tissue reticulum, a very little collagen about the larger blood vessels, a few well-differentiated adult neuroglia fibrillae (Fig. 19), and numerous embryonic neuroglia processes which were demonstrable only by Hortega's fourth variant (Fig. 20). No neurofibrillae were to be found. A few nuclei of dumb bell shape were seen, presumably dividing by amitosis. Mitotic nuclear figures were common.

The period of improvement in this case was of unusually short duration, shorter indeed than in any other case in the series in which

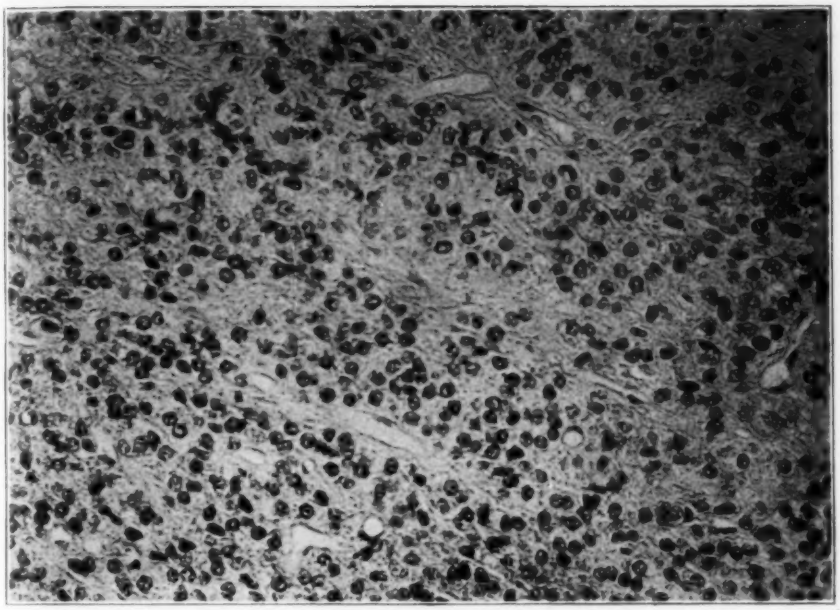

Fig. 18 (Case 9).—Abundant internuclear material which does not stain with phosphotungstic acid hematoxylin; × 300.

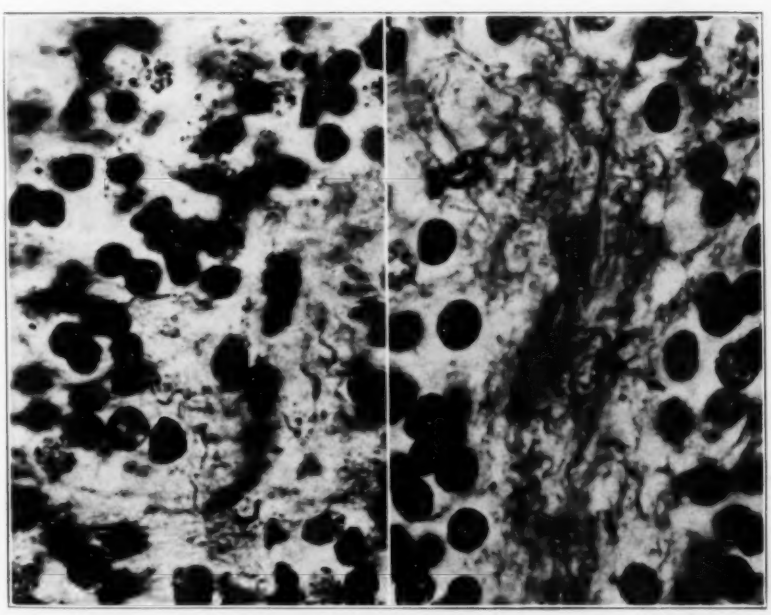

Fig. 19 (Case 9).—Adult neuroglial fibrillae shown by Hortega's first variant; × 850.

Fig. 20 (Case 9).—Embryonic glial processes shown by Hortega's fourth variant; × 850.

the patient survived operation, as can be seen from the table. In one case, the first in the Brigham Hospital list (Case 6), the patient had an extraordinarily long survival period, twenty-one months, from the time of the first operation, which amounted merely to a decompression. At two subsequent operations, the tumor, which the decompression had permitted to attain an enormous size, was radically extirpated. These repeatedly successful operations doubtless account for the long survival period.

It will be seen also that the next three patients that were operated on (Cases 11, 12 and 13) had survival periods of nine, ten and sixteen months, respectively, although in the last of these the operation amounted to little more than a decompression with the removal of a fragment of tumor for histologic examination.

As the table makes evident, radiation was first employed as a supplementary measure to the operation in Case 14, and immediately the survival periods began to lengthen. Radiation, however, has not accomplished all that might be desired, although the results have on the whole been much more favorable than by operation alone. The history of the longest survival—a story not yet completed—is as follows:

Midcerebellar medulloblastoma arising from above the fourth ventricle. Operation with subsequent radiation and survival for more than four years.

CASE 17.—*History.*—On Feb. 9, 1921, Jack H., aged 6 years, a schoolboy, referred by Dr. E. Koplik of New York City, was admitted to the hospital with the complaint of headache, vomiting, crossed eyes and unsteadiness.

In July, 1919, having previously been in good health, he began to have attacks of vomiting. These were treated as gastric attacks. There were no headaches. In May, 1920, he complained of double vision. Two months later, he had his first severe frontal headache, which lasted for two days. Similar bad headaches recurred, and soon were practically constant. In some of the last attacks he was unconscious for a few minutes, with retracted head and rigid body. Some unsteadiness seems to have been present for about two years. The parents thought the boy was clumsy. For the past three months there had been definite staggering with inability to walk alone.

Examination.—On admission the patient was a bright boy with an enlarged head which gave a cracked pot sound on percussion. A bilateral choked disk was present, with an elevation of 4 diopters, hemorrhages and considerable secondary atrophy. There was paresis of the left external rectus muscle, marked nystagmus on looking to either side, and incoordination of cerebellar type involving all extremities. He was able to take a few steps, but his gait was most unsteady.

Course of Illness.—On Feb. 14, 1921, the usual bilateral suboccipital exploration was made, revealing a median cerebellar tumor projecting down inside the posterior cistern through the foramen magnum. In order to expose the lower margin of this projection, it was necessary to remove the posterior arch of the atlas and to carry the dural incision down to the axis. The appearance is roughly shown in the accompanying sketch made at the time (Fig. 21).

It was hoped that the tumor might be tilted upward, but it was found that the growth could not be separated from the medulla in the region of the calamus because of the presence of a large artery which crossed this part of the lesion. Several portions of the soft tumor were removed for histologic study; the bleeding was checked and the wound closed.

The boy recovered promptly. Headache and vomiting ceased, and he was discharged on March 11, 1921, in excellent condition, with few traces of his former symptoms. He subsequently received about five roentgen-ray treatments. He returned on July 16, 1923, at which time he showed no symptoms of any cerebellar disturbance. He remained free from symptoms for four years. He attended school, engaged in sports and was apparently normal in all respects. He reentered the hospital on March 9, 1925, four years after the operation, with slight evidence of the return of his former symptoms—some vomiting and headache but no cerebellar signs (Fig. 22).[9]

Pathologic Description.—The material removed at operation was fixed in Zenker's fluid, and consequently impregnation methods for embryonic glia and neurofibrillae were precluded. The tumor was diagnosed at the time as a neurocytoma.

A reexamination showed that the growth consisted of a disorderly mass of cells with oval nuclei almost similar to those described in the other cases (Fig. 23). The nuclei had abundant chromatin. There was considerable intercellular material, though less than in the preceding case, consisting for the most part of thick processes of the cells and occasional well developed adult neuroglia fibrillae (Fig. 24). Connective tissue was confined to the walls of rare blood vessels. The centrosomes could not be seen. Mitotic figures were frequent. It was impossible to stain for neurofibrillae, but no cells resembling neuroblasts were to be found.

Comment.—The case is an example of what may be accomplished for even such serious lesions as those which comprise this series. A new growth could hardly be situated in a position more dangerous to life, and when it is a rapidly growing lesion, as are the medulloblastomas, the

9. This case is important enough to deserve this additional footnote. On readmission, after a four year interval, one would hardly have believed that there had ever been a cerebellar operation. The occipital bone had been almost entirely reformed, and there was no suboccipital protrusion. The patient had no evident pressure symptoms other than slight subjective discomforts, and no choked disk. There were practically no cerebellar signs. Nevertheless, under the belief that there must have been a reactivation of the quiescent growth, on March 23 he was given a deep therapeutic roentgenization of the cerebellum. A few hours later, he began to have severe headaches and vomited, and within twelve hours had become stuporous. His stupor increased, with a slow pulse and Cheyne-Stokes respiration. As a life-saving measure, under local anesthesia, the old cerebellar flaps were reflected, the new-formed bone removed, and a huge, softened median cerebellar growth was easily detached. This exposed the greatly widened floor of the fourth ventricle, and one could look into the distended iter from which fluid escaped in abundance. The child had a very close call from a postoperative hyperthermia, but from this he recovered, had a good convalescence, and was discharged. It is hoped that he will have at least another four-year period of relief, if indeed the growth may not have been completely destroyed by this radiation.

fact that one should occasionally be able to prolong life and at the same time make it worth living by any therapeutic measure whatsoever is enough to encourage us to persist in our efforts. It is probable that with our present-day knowledge of the symptomatology of these lesions, of their pathologic nature, of the limits to which the operation should be confined, namely, largely to decompressive measures, and of the beneficial

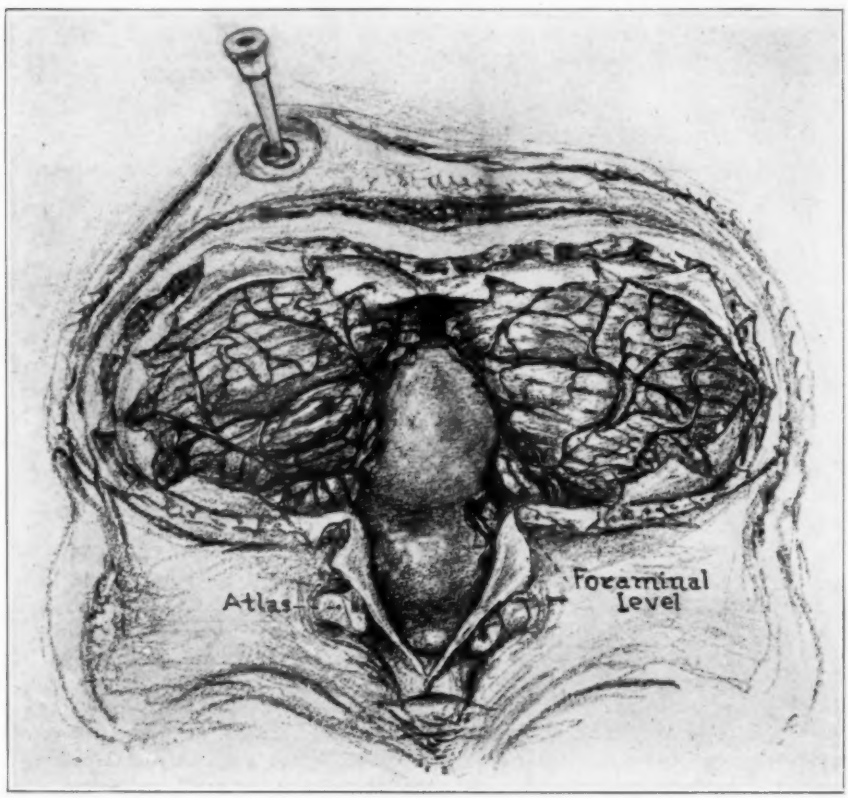

Fig. 21 (Case 17).—General appearance and situation of tumor as exposed at operation.

effects of radiation, that future series of cases in the same or other hands will show much more encouraging results.

CLINICAL SYNDROME

The syndrome of these cases might be easily forecast from a knowledge of the primary site of the tumor and of its histologic nature. Taking the case histories as a whole, the inaugural symptoms in most instances were those of increased intracranial tension, the evidence of which was likely to be abrupt and to have been present for comparatively

few months before the patient's admission to the hospital. It is true that the histories occasionally tell of an occasional headache of obscure origin, usually attributed to some gastric upset, for a year or so before, but the usual story is one which can probably be ascribed to a comparatively abrupt and more or less complete block of the cerebrospinal fluid with internal hydrocephalus. These symptoms are headache, projectile vomiting and the rapid appearance of choked disk. Since the patient is usually preadolescent, a separation of the cranial sutures, which gives the characteristic cracked pot-sound to the skull on percussion, is likely to be present.[10]

Fig. 22 (Case 17).—Patient after four years, showing absence of any suboccipital bulging.

In the general run of cases, the symptoms of primary pressure which may be properly ascribed to the hydrocephalus may overshadow

10. One case in the series (Case 26) shows, nevertheless, that a tumor of considerable size may be completely latent. The patient was a young man, aged 22, who supposedly had had no symptoms of any intracranial trouble until sixteen days before his admission to the hospital, when he had been kicked on the head in a football scrimmage. He was supposed to have a post-traumatic lesion; a lumbar puncture was performed, and subsequently a subtemporal decompression, which apparently precipitated his death. A medico-legal examination disclosed an entirely unsuspected midcerebellar medulloblastoma of characteristic histology.

the signs of cerebellar involvement. However, there is almost always a history of a staggering gait, and by the time of the patient's hospital admission, a full-blown cerebellar syndrome is usually apparent. The ataxia is likely to be more evident in the lower extremities than in the upper, and most of the children were unable to stand alone or to take steps without assistance. In several of them there had been a history of cerebellar seizures with retraction of the head, respiratory difficulty and other symptoms which suggested a basilar meningitis.

In the discussion of one of the cases attention has been called to the fact that nystagmus has been an inconspicuous feature of the cerebellar

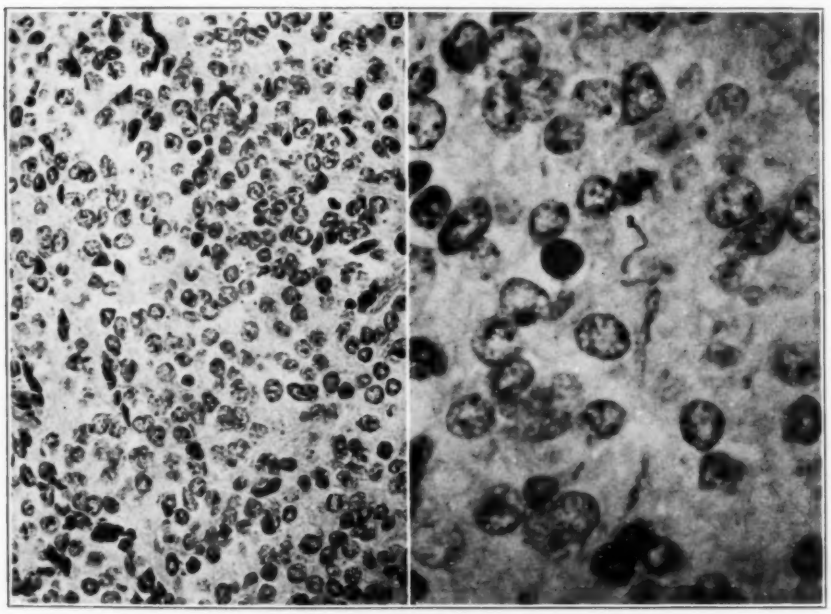

Fig. 23 (Case 17).—A section of tumor stained with methylene blue eosin; × 300.

Fig. 24 (Case 17).—Adult neuroglial fibrillae shown by neutral ethyl violet orange G. stain; × 850.

syndrome, as might possibly be expected from the midline position. However, diplopia has almost always been present, and in perhaps more than the usual number of cerebellar cases there has been a bilateral abducens palsy. In three or four cases, also, there has been a slight weakness of the face on one side.

The average age in the twenty-nine cases is 10 years. Five cases occurred when the patients were in the twenties; with these exceptions all were below 15 years. Twenty out of the twenty-nine cases occurred during the first decade of life.

THE PATHOLOGY OF THE LESION

As stated, in all the cases, the tumor seems to have originated over the roof of the fourth ventricle and to have developed as a central intracerebellar lesion. The lesions have appeared macroscopically both at operation and at necropsy to be fairly well circumscribed, though histologic study invariably has shown invasion of the surrounding cerebellar tissue. When the neoplasm appears on the surface (Fig. 1), it first becomes evident between the tonsils of the cerebellum, and experience at the operating table (Fig. 21) has shown that the growth is particularly likely to crowd its way downward through the foramen magnum. The fourth ventricle of course is greatly enlarged and deformed, and an unattached tongue of the tumor in one case extended even through the dilated iter into the third ventricle. In four instances, the tumor apparently had "infected" the subarachnoid spaces, three times forming metastases in the spinal region and once (Case 5) spreading widely through the leptomeninges over the base of the cerebellum and even over the surfaces of the cerebral hemispheres.

Histologically, these tumors are composed of rounded or pear-shaped, sometimes spindle-shaped cells, with scanty cytoplasm and big oval nuclei containing an abundant network of chromatin. On low magnification, the cells as a rule appear as a loose structureless mass, but the nuclei occasionally show architectural disposition and may form pseudo-rosets (Fig. 25) or lie in strands suggesting the arrangement of nuclei in a spindle cell sarcoma. Again, they may lie grouped around irregular spaces and acquire a sort of palisade arrangement (Fig. 26). These variations, which may be seen in different parts of the tumor, are of no essential importance.

From one or sometimes from both poles of the cells, there emerges an elongated process at the base of which a centrosome, surrounded by a clear halo, may often be seen. This usually is a single granule (Fig. 27), though occasionally it shows as a diplosome. These processes make up the bulk of the internuclear material, in which occasional thin-walled blood vessels may be found; and such delicate connective tissue as is demonstrable by Perdrau's method is usually confined to their walls (Fig. 28). Such variations as exist in the gross microscopic picture are consequently due to the relative abundance and arrangement of the cell processes rather than to the presence of any connective tissue stroma.

That the internuclear material is composed largely of the processes of embryonic glia cells can be shown by its ready impregnation with Achúcarro's tannic silver method (Fig. 29), as well as with Hortega's fourth variant of this method when the material has been suitably fixed. In material fixed in Zenker's fluid occasional adult neuroglia fibrillae can

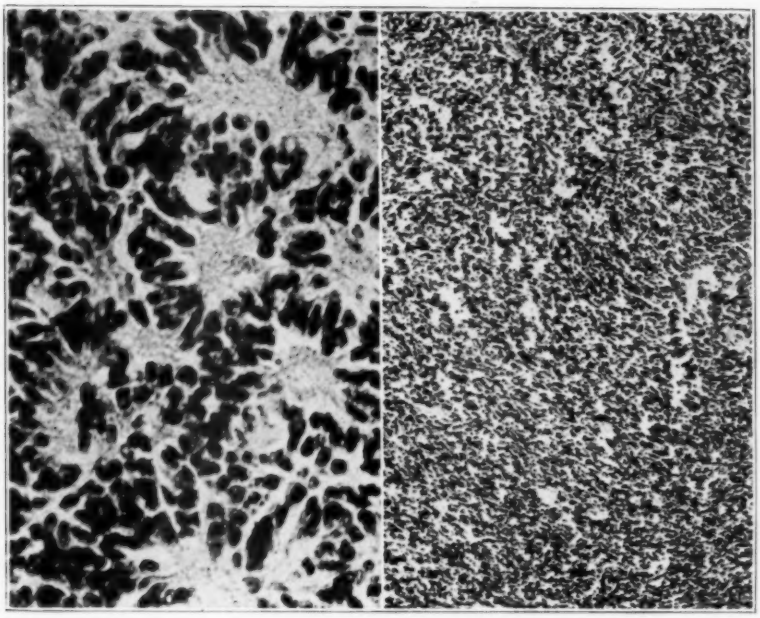

Fig. 25 (Case 18).—Ball-like pseudorosets of the medulloblastoma. Hematoxylin and eosin stain; × 600.

Fig. 26 (Case 18).—Showing irregular areas free of nuclei, the nuclei forming a sort of palisade around them. Neutral ethyl violet-orange G. stain; × 80.

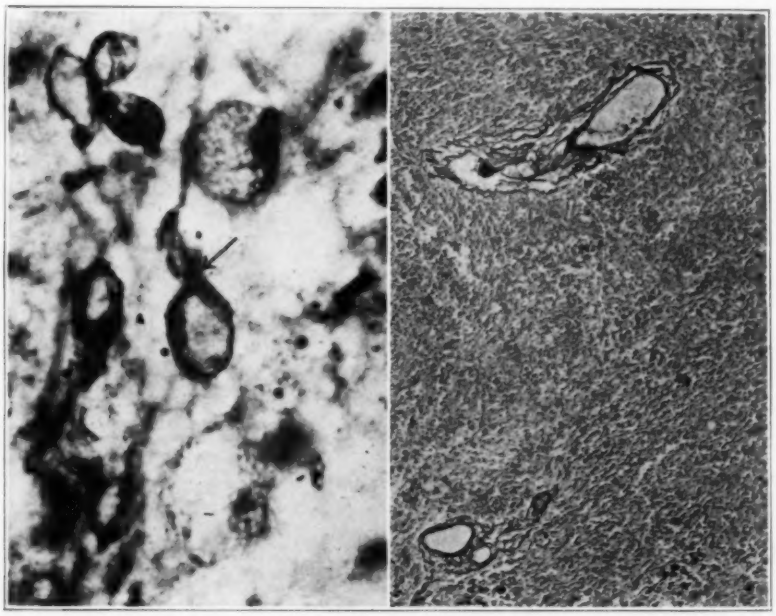

Fig. 27 (Case 10).—Unipolar spongioblast with single centrosome, at base of process, surrounded by clear halo. Perdrau's method, modified; × 850.

Fig. 28 (Case 12).—Usual arrangement of connective tissue in these tumors, surrounding small blood vessels. Perdrau's method; × 80.

be stained by the usual methods. No neurofibrillae are demonstrable by any of the appropriate stains, whatever the fixation.

ORIGIN AND NATURE OF THE TUMOR CELLS

Many of the cells are so undifferentiated that their nature is not evident from their microscopic structure. If of ectodermal origin, they must be akin to the "indifferenten Zellen" of Schaper,[11] or as we prefer to call them, medulloblasts. It is well known that the cells forming the cerebellum migrate in an extraordinary way during embryonic life, and it would seem to be not improbable that in this situation groups of cells might become isolated and retarded in their development.

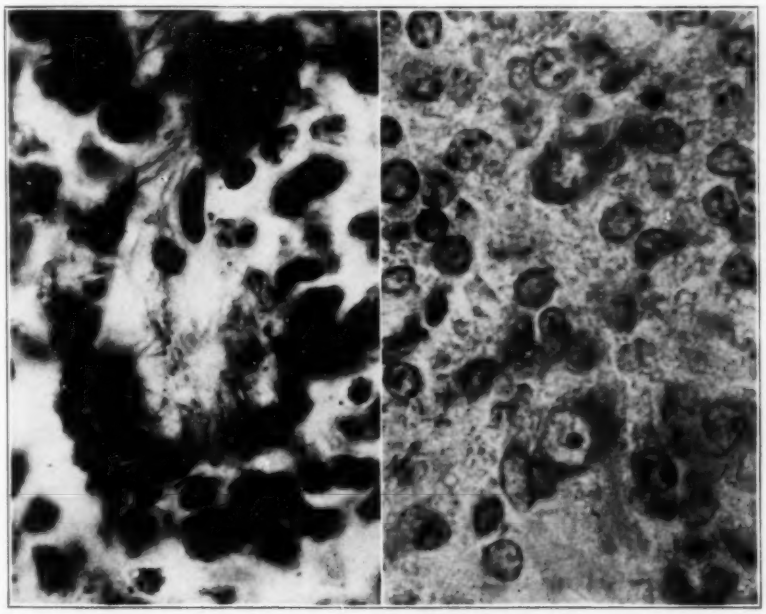

Fig. 29 (Case 12).—Typical ball of cells, showing delicate fibrillae impregnated by Achúcarro's tannic silver method; ×850.

Fig. 30 (Case 19).—To show what are supposed to be neuroblasts, with large nuclei containing a heavy nucleolus. Methylene blue-eosin stain; ×850.

Should these isolated cellular groups differentiate, a heterotopic malformation would result. Pfleger[12] found such heterotoptic cellular groups in the region of the fourth ventricle in seventy-five out of 400 supposedly normal cerebella. If such an isolated and retarded group of

11. Schaper, A.: Die Frühesten Differenzirungsvorgänge im Centralnervensystem, Arch. f. Entwklngsmechn. **5**:81, 1897.

12. Pfleger: Centralbl. f. d. med. Wissensch., 1880, No. 26, p. 468.

undifferentiated cells should undergo a neoplastic transformation, just such a tumor as we have described might be expected to result.

Schaper believed his indifferent cells capable of differentiation either into neuroblasts or spongioblasts. In one restricted area in one of our tumors, cells were found which showed the characteristics of neuroblasts. The tissue in this case had been fixed in Zenker's fluid so that it was impossible to obtain positive evidence of this fact by impregnation with silver. Nevertheless, the large circular nuclei, containing no scattered granules of chromatin and a single heavy nucleolus surrounded by heavily stained cytoplasm, can scarcely be interpreted otherwise than as belonging to neuroblasts (Fig. 30). An attempt to stain tigroid substance in their cytoplasm with the methylene blue-erythrosin method of Held was not successful.

Although a few of the neoplastic cells are, therefore, neuroblasts, many more are spongioblasts, their structure and staining reactions being identical with those of the unipolar spongioblasts of the developing central nervous system, as the preceding descriptions show. Their spongioblastic nature is further evidenced by the fact that neuroglia fibrillae are occasionally differentiated within them, as is shown by the ordinary staining methods for such fibrillae. The differentiation of adult neuroglia fibrillae seems to be accompanied by other changes in the cell, for they seem to come from the neighborhood of smaller, more heavily stained nuclei, while the more delicate embryonic processes come from larger nuclei which are more vesicular. An attempt to show these differences has been made in Figure 31. In some of these more differentiated cells, the development has gone so far that when impregnated by Cajal's gold sublimate method they appear as typical astrocytes. It might be supposed that such astrocytes as are shown in Figure 32, from one of these tumors, were merely inclusions of normal tissue cells in the new growth. This supposition seems untenable for the reason that these cells show no signs of degeneration; that they are found in the very heart of the tumor, and not alone in the periphery; and that they may be seen in all stages of differentiation.

There can be no doubt, therefore, that although the majority of the neoplastic cells are potential neuroglia cells, some are potential neurones, and it is on this basis that the designation of medulloblastoma has been adopted.

INVASION OF THE MENINGES BY MEDULLOBLASTOMAS

It has long been remarked that tumors of the fourth ventricle are prone to invade the meninges. There can be collected from the literature numerous cases of this invasion due to what we regard as undifferentiated medulloblastomas. The first was recorded by Ollivier (1837). Other reports have followed by Ross (1877), Schultze (1880), Turner

(1886), Richter (1886), Coupland and Pasteur, Case 2 (1887), Busch (1896), Nonne (1897), Weaver (1898), Michael (1902), Spiller and Hendrickson (1903), Rindfleisch (1904), Dercum (1906), Rosenblath (1906), Rach (1907), Martens and Seiffert (1908), Batten (1908-9), Wimmer and Hall (1913), Ford and Firor, Case 2 (1924). There are doubtless others. This list does not take into account the numerous cases of medulloblastomas or spongioblastomas of the cerebral hemispheres which have invaded the subarachnoid spaces, such as the cases of Westphal, Lenz, Löwenburg, Askanazy, Strauss and Globus, etc. We have had an example in our own series (which, in addition to the

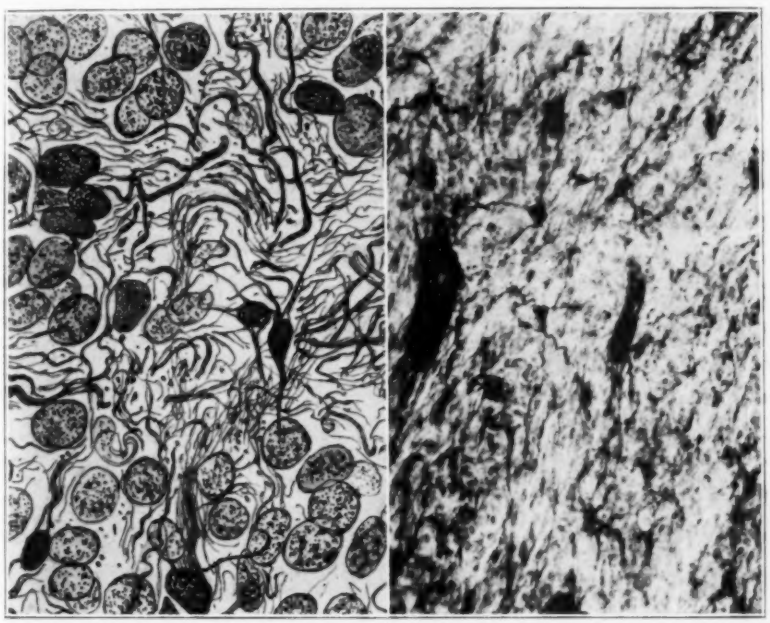

Fig. 31 (Case 19).—Result of differentiation on the nuclei of the cells. Hortega's fourth variant; × 850.

Fig. 32 (Case 22).—Astrocytes impregnated by Cajal's gold sublimate method; × 300.

twenty-nine examples of this report, comprises five cases of undifferentiated medulloblastomas of the cerebral hemispheres) of such a widespread extension. Numerous examples of primary medulloblastomas of the spinal cord which have invaded the meninges might also be added (Fischer, Grund, Schlesinger, Schlagenhaufer, etc.).

In our present series of twenty-nine cerebellar cases, the tumor in three of them had invaded the spinal meninges, while in the fourth (Case 5) it had spread widely over the cerebellar and cerebral hemispheres through the leptomeninges.

Most lesions of this kind have been described in the older literature under the term sarcoma or sarcomatosis, and more recently gliosarcoma, encephaloid sarcoma, etc. They are in reality composed of embryonic medullary cells, as has been remarked by many observers. We have definite reasons to believe that they are clearly distinguishable from the actual primary sarcoma of the brain, which is an exceedingly rare tumor and presumably must come from the walls of the blood vessls.

TREATMENT

The ultimate object of a study of this kind is the improvement of our therapeutic procedure for a given type of tumor. This can only come from increased knowledge of the exact situation, nature and manner of growth of the lesion. The table shows that attempts to extirpate these particular tumors totally are futile, and that even exposure and decompression may be accompanied by a high mortality. This is not a matter for surprise in view of the hazardous situation of the lesion which overlies the fourth ventricle and often projects for some distance down the spinal canal through the foramen magnum. That the operative mortality has not been greater may perhaps be taken as a matter for congratulation.

The temptation will always be present for the surgeon to attempt an enucleation in view of the apparent encapsulation of the tumor when approached from its posterior surface, but it is safe to say that a conservative attitude in this respect is the course of wisdom.

Our present feeling is that a simple suboccipital decompression followed by persistent roentgen-ray therapy offers the best results. The patients who survived the operation and were not given treatment with the roentgen-ray had an average survival of only seven months, while those treated by radiation, including only those who have died, have had an average survival period of more than nineteen months. Three of the patients are still alive. The tabulation of cases conveys of course no idea of the enormous subjective relief offered to these unfortunate children by the decompression during the postoperative survival period. The experience with the case last reported (Case 17) shows what may result and gives hopes for these desperate cases in the future.

SUMMARY

1. A series of twenty-nine centrally placed cerebellar tumors, arising from above the roof of the fourth ventricle and occurring mainly in children, has been described.

2. For these tumors the term medulloblastoma is proposed.

3. Evidence is submitted that they are composed mainly of indifferent cells, analogous to those described by Schaper in the developing cerebellum, and that most of these cells are potential neuroglia.

4. The surgical experiences indicate that the best method of treatment consists of a suboccipital decompression followed by persistent roentgen-ray therapy.

DISCUSSION

DR. HARVEY CUSHING: When Dr. Bailey and I began work on this particular group of tumors, we were unaware that they had previously been described as spongioblastomas. Indeed, it was not until we saw the program of the present meeting that we learned not only that Dr. Globus and Dr. Strauss were working on the same subject as ourselves, but also that they had already baptized the child. In view of their priority in this matter, we have most willingly acceded to the petition by Dr. Globus that his paper should be allowed to precede rather than to follow our own. This was as it should be. But, unfortunately, from what Dr. Globus has said and from the pictures he has shown, I fear we would not recognize our own child in anything but the name. It is futile, I think, to inflict on the Society any further discussion in this matter, and I propose that Dr. Globus and Dr. Strauss, Dr. Bailey and I foregather in some quiet antechamber and thrash this matter out together rather than to take the Society's time by doing so in open meeting.

Dr. Bailey has also prepared a diagram to indicate from what cells these tumors arise; and though it agrees in many points with the diagram Dr. Globus has presented, we favor the inclusion of two types of spongioblasts. From only one of these cell types do the tumors with which we are concerned take their origin, namely, from the very early spongioblasts or medulloblasts of the nervous system which antedate any differentiation into neuroglia. Dr. Globus and Dr. Strauss, I surmise, are dealing with a tumor much more akin to the true neuroglial tumor, for some of their slides show definite neuroglia fibers. All such tumors we have excluded from our group. We may possibly have leaned over backward in our effort to exclude all other tumors than those of one definite type, and our friends from New York may have leaned in the other direction in an effort to include as many tumors as they could within the grouping which they had made. Their tumors, moreover, appear to be cerebral in origin whereas ours with few exceptions have been found in the cerebellum.

Our tumors represent a type with which we have been familiar for a long time. As stated, they are tumors which usually give symptoms in the first decade of life, and they are often spoken of as tumors of the fourth ventricle. We are now so familiar with them that we could almost be certain of the diagnosis from gross appearances alone, without waiting for histologic verification. In addition to these twenty-nine there have been five with a similar histologic picture from other parts of the brain, but they are in some ways less distinctive than those of the midcerebellar type.

We are also familiar with the tumors which Dr. Globus has shown us. They represent a definite type of neoplasm, perhaps the most common of all gliomas, and include those which in former days were called gliosarcomas. Just what we may decide about them in the matter of terminology I cannot be sure; but at least either Drs. Globus and Strauss, or Dr. Bailey and I will have to recede from our proposed terminology and agree on some different term for these obviously different types of tumor.

Our midcerebellar gliomas are, I think, far less malignant lesions than those which Dr. Globus has presented, being more dangerous to life from their situation than from their malignancy. They, on the other hand, are more malignant than the ependymomas arising in this region — tumors of which Dr. Bailey has already made a detailed report.

It is for us neurosurgeons most important that we should know all that we possibly can regarding the different types of gliomas, which represent about 40 per cent. of all of our intracranial tumors. The prognosis of some of them is as favorable as that of any tumors of the nervous system; the prognosis in some extremely unfavorable. It is not until we can begin to regroup them, and this process carries with it the necessity of renaming them, that we can make any great advances. To make advances it is necessary that we, one and all, understand what the other man is talking about. The same name for two different conditions will hinder rather than help, and I trust that by the time of our next meeting Dr. Globus, Dr. Strauss, Dr. Bailey and I may have something further to say on the matter before the Society.[13]

Dr. Percival Bailey: I think the whole discussion hinges on the fact that we are calling two different things by the same name. Dr. Cushing and I make no claim to having invented the word "spongioblastoma" and are willing to give Dr. Globus credit for this excellent term.

The last lantern slide which we showed was copied from Castro's article on the evolution of the spongioblast. We are struck by the resemblance of the tumor cells to what Castro called the dislocated epithelial corpuscle.

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13. We at first decided to distinguish the two types by calling our tumors *spongioblastoma indifferentiale* and the tumor of Globus and Strauss *spongioblastoma multiforme;* but on more mature consideration it has seemed more appropriate to the tumors of the type we described to term them *medulloblastomas* and thus to avoid any further confusion. Hence the title of our paper has been changed.

ELECTRICAL CONDUCTIVITY OF THE SPINAL FLUID*

JOHN L. ECKEL, M.D.

BUFFALO

Only a small amount of research work has been done on the conductivity of the spinal fluid. Polányi [1] made some estimations on fluids from cases of hydrocephalus; Levinson [2] made some studies from a few other conditions, and Crile, Hosmer and Rowland,[3] in their work on conduction of animal tissues, included the spinal fluid from a number of rabbits.

In this investigation, I have attempted to obtain fluids from as many different conditions of the central nervous system as possible. In some, the number of cases has been too small to permit definite conclusions. However, in the more common diseases of the nervous system, the series is fairly large. These fluids, were obtained, to a large extent, from the superintendents and staff of the Craig Epileptic Colony, Sonyea, N. Y., the Buffalo and Gowanda State Hospitals, and the Buffalo City Hospital. The fluids were collected in sterile tubes, free from electrolytes, sent at once to the laboratory, and tested soon after arrival. Conductivity tests were made altogether on over 360 spinal fluids. All fluids were obtained by lumbar puncture. The following instruments were used: a typical Wheatstone bridge, made up of a Kohlrausch slide wire and a three-dial resistance coil, with a telephone receiver connected across the ends of the slide wire; a hummer; a constant temperature bath set at 25 C. and a special conduction cell. This cell is made from glass, the electrodes being platinum, $\frac{5}{16}$ inch in diameter, connected by a tube 1 inch in length and with an inside diameter of $\frac{5}{32}$ inch. This cell required slightly more than 1 c.c. of fluid. In measuring the resistances, three cells, all having about the same dimensions, were used; but it was soon found that there was a slight difference in their resistance measurements. Cell 1 was slightly higher and Cell 3 slightly lower than Cell 2. It was also observed that this difference in Cells 1 and 3 ran parallel, or nearly so, throughout the

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* Read at the Fifth Annual Meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 29 and 30, 1924.

1. Polányi: Beiträge zur Chemie der Hydrocephalüsflussigkeit, Biochem. Ztschr. **34**:205, 1911.

2. Levinson: Cerebro-Spinal Fluid, Ed. 2, St. Louis, C. V. Mosby Company, 1923, pp. 106 and 150.

3. Crile, G. W.; Hosmer, Helen R., and Rowland, May F.: The Electrical Conductivity of Animal Tissues under Normal and Pathological Conditions, Am. J. Physiol. **60**:59-105, 1922.

work. Therefore, we concluded in our summary to use the readings found with Cell 2, as these more nearly represented the average of the three cells.

These cells were cleansed with double distilled water, rinsing them several times, and this was followed by the use of absolute alcohol, and later by ether. Several readings were made on each fluid, and the average was taken as the final result. All fluids showing any contamination or containing blood were discarded.

To convert the resistance of the fluids expressed in ohms into specific conductance, it was necessary first to determine the cell con-

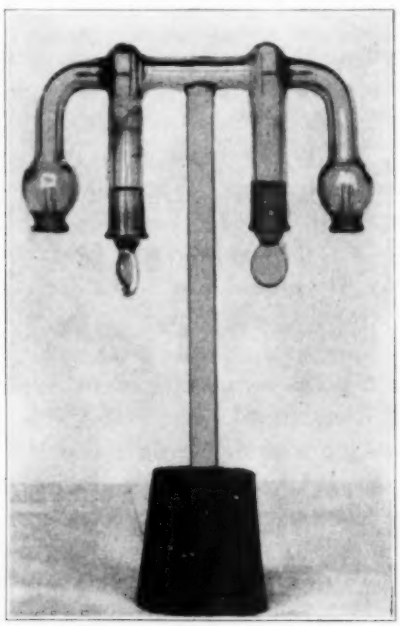

Fig. 1.—Cell used in making conductivity tests. The platinum electrodes are 5/16 inch in diameter; connecting tube, 1 inch long; diameter of tube, 5/32 inch; capacity, slightly over 1 c.c.

stant. For this purpose, the technic of H. and E. Parker,[4] using a 0.1 D[5] potassium chlorid solution at 25 C. They found the specific conductance of this solution under those conditions to be 0.01285.

In the preparation of this 0.1 D potassium chlorid solution, 7.479 gm. of fused potassium chlorid were weighed in the air and added to each

4. Parker, Henry C., and Parker, E. W.: The Calibration of Cells for Conductance Measurements. III. Absolute Measurements on the Specific Conductance of Certain Potassium Chloride Solutions, J. Am. Chem. Soc. **46**:312 to 335, 1924.

5. D = 1 cubic decimeter solution.

1,000 gm. of distilled water, also weighed in the air. By this method, no correction for the density of the water was necessary.

The solution having been prepared, the resistance of the distilled water used in the preparation of the solution was then measured at 25 C. and called R_W. After cleansing the cell thoroughly, the potassium chlorid solution was placed in it, and its resistance measured at 25 C. and called R_S.

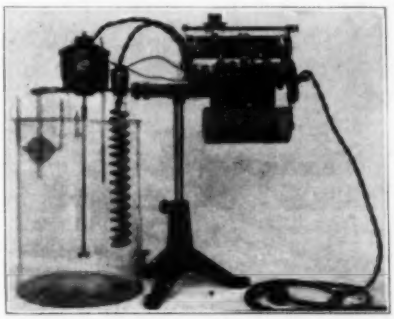

Fig. 2.—Constant temperature bath.

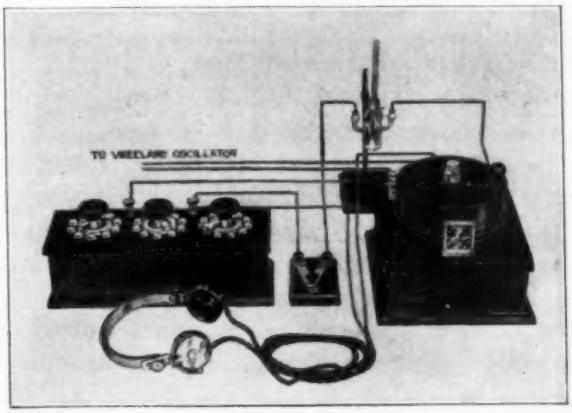

Fig. 3.—Wheatstone bridge, resistance coil and telephone receiver.

The cell constant C was found from the equation:

$$C = 0.01285 \left[0.01285 + \frac{0.01285 \times R_s}{R_w} \right] \times R_s.$$

The second member in parenthesis corrects for the specific conductance of the water; this was found to be almost negligible, but in this work it has been corrected.

Having established the cell constant, the specific conductance L was found from the following equation: $L = \frac{C}{R}$ in which R is the resistance of the spinal fluid measured at 25 C. in the same cell.

In the preparation of the solution and in the estimation of the total solids in numerous specimens of spinal fluids, I had the assistance of Dr. George Pucher of the Department of Biochemistry, University of Buffalo, and in the adjusting of apparatus and the interpretation of the findings I have had the constant assistance of Professors Moore and Cooke of the Department of Physics, University of Buffalo.

The conductivity of the spinal fluid was found by a number of estimations to depend on the salt content of the fluid. These salts are all highly ionized, and the conductivity is the relative measure of the total ionized solids present in the fluid. Sodium chlorid is present in the largest amount, while potassium, magnesium, iron, phosphorus and other electrolytes are present in smaller quantities. The amount of globulin and albumin present in the various fluids, while it does not

TABLE 1.—*Specific Conductance in Normal Fluids*

Case No.		Case No.		Case No.		Case No.	
1	0.01461	8	0.01549	15	0.01495	21	0.01513
2	0.01452	9	0.01508	16	0.01507	22	0.01495
3	0.01480	10	0.01504	17	0.01503	23	0.01496
4	0.01481	11	0.01517	18	0.01508	24	0.01537
5	0.01446	12	0.01499	19	0.01526	25	0.01471
6	0.01519	13	0.01530	20	0.01518	26	0.01425
7	0.01476	14	0.01501				

Maximum, 0.01549; minimum, 0.01446; average, 0.014953.

materially change the conductivity, has some depressing effect. Gram,[6] in his work on conductivity of the blood serum, found the protein content to diminish the resistance somewhat, and he established an equivalent conductance for the protein content, which, although small, did show a definite resistance of its own. I have not made the estimation of the protein content in each fluid in this series, leaving that for subsequent investigation.

The normal fluids in this series were obtained from patients having other than neurologic signs or symptoms; none of these fluids contained globulin, and none showed an abnormal cell count. As will be seen in Table 1, there was considerable variation in the conductance of these fluids, all of which was found to be due to variation in the salt concentration of the fluid. Nearly all the pathologic fluids, of which the series contained ten or more specimens, showed an average conductance less than the normal. In a few in which the number was small, the conductance was slightly higher than the average normal.

6. Gram, H. C.: Observations on the Regulation of Osmotic Pressure (Conductivity, Chlorides, Freezing Point, and Proteins of Serum), J. Biol. Chem. **56**:593 to 624, 1923.

Table 2 represents the specific conductance of cerebrospinal syphilis, exclusive of general paralysis and tabes. Here again about the same degree of variation is found as in the normal fluids, but the average is slightly lower than that of the normal. This series contained fifty-seven cases.

TABLE 2.—*Specific Conductance in Cerebrospinal Syphilis*

Case No.	Case No	Case No.	Case No.
1.....0.01508	16.....0.01476	30.....0.01495	44.....0.01457
2.....0.01509	17.....0.01501	31.....0.01473	45.....0.01475
3.....0.01472	18.....0.01501	32.....0.01478	46.....0.01470
4.....0.01423	19.....0.01449	33.....0.01514	47.....0.01475
5.....0.01474	20.....0.01522	34.....0.01495	48.....0.01453
6.....0.01508	21.....0.01492	35.....0.01453	49.....0.01463
7.....0.01474	22.....0.01574	36.....0.01460	50.....0.01537
8.....0.01508	23.....0.01495	37.....0.01460	51.....0.01476
9.....0.01472	24.....0.01488	38.....0.01524	52.....0.01482
10.....0.01474	25.....0.01510	39.....0.01478	53.....0.01482
11.....0.01503	26.....0.01478	40.....0.01514	54.....0.01421
12.....0.01507	27.....0.01473	41.....0.01486	55.....0.01478
13.....0.01503	28.....0.01478	42.....0.01455	56.....0.01460
14.....0.01503	29.....0.01441	43.....0.01475	57.....0.01570
15.....0.01476			

Maximum, 0.01524; minimum, 0.01432; average, 0.014853.

TABLE 3.—*Specific Conductivity of Tabetic Fluids*

Case No.	Case No.	Case No.	Case No.
1.....0.01481	11.....0.01568	21.....0.01549	31.....0.01471
2.....0.01502	12.....0.01522	22.....0.01522	32.....0.01487
3.....0.01480	13.....0.01508	23.....0.01508	33.....0.01509
4.....0.01456	14.....0.01498	24.....0.01487	34.....0.01455
5.....0.01530	15.....0.01486	25.....0.01489	35.....0.01551
6.....0.01455	16.....0.01508	26.....0.01498	36.....0.01501
7.....0.01553	17.....0.01487	27.....0.01474	37.....0.01548
8.....0.01504	18.....0.01466	28.....0.01478	38.....0.01505
9.....0.01486	19.....0.01460	29.....0.01483	39.....0.01482
10.....0.01424	20.....0.01485	30.....0.01474	

Maximum, 0.01568; minimum, 0.01424; average, 0.014928.

TABLE 4.—*General Paralysis*

Case No.	Case No.	Case No.	Case No.
1.....0.01482	10.....0.01462	18.....0.01533	26.....0.01498
2.....0.01446	11.....0.01510	19.....0.01462	27.....0.01460
3.....0.01506	12.....0.01476	20.....0.01561	28.....0.01482
4.....0.01465	13.....0.01479	21.....0.01482	29.....0.01470
5.....0.01533	14.....0.01471	22.....0.01482	30.....0.01482
6.....0.01456	15.....0.01485	23.....0.01482	31.....0.01482
7.....0.01501	16.....0.01450	24.....0.01520	32.....0.01508
8.....0.01462	17.....0.01484	25.....0.01474	33.....0.01518
9.....0.01502			

Maximum, 0.01561; minimum, 0.01446; average, 0.014865+.

In Table 3 is represented the conductance in a series of tabes cases of all types. It was rather difficult to differentiate the degree of activity in these cases, so they have all been classed under one heading. By this method, no doubt there is a greater variation in the conductance than if the cases had been carefully classified into the various degrees of activity of disease process. The average conductance is found to be nearly that of the normal fluid.

In Table 4 is shown the conductance of thirty-three cases of well developed general paralysis. About the same degree of variation is shown as in the previous tables, with the average near to that of the normal.

In Table 5 is represented a series of cases of dementia praecox, manic-depressive phychoses of both phases and involutional melancholia. The dementia praecox cases show a conductance slightly below the normal fluid, while the manic and involutional melancholia fluids are

TABLE 5.—*Specific Conductance in Certain Mental Diseases*

Dementia Praecox		Manic-Depressive Psychoses	Involutional Melancholia
Case No.	Case No.	Case No.	Case No.
1.....0.01495	13.....0.01513	1.....0.01518	1.....0.01517
2.....0.01465	14.....0.01488	2.....0.01507	2.....0.01519
3.....0.01460	15.....0.01461	3.....0.01522	3.....0.01517
4.....0.01532	16.....0.01504	4.....0.01485	4.....0.01505
5.....0.01480	17.....0.01472	5.....0.01478	5.....0.01456
6.....0.01482	18.....0.01441	6.....0.01509	6.....0.01462
7.....0.01542	19.....0.01461	7.....0.01478	7.....0.01549
8.....0.01501	20.....0.01512	8.....0.01518	8.....0.01528
9.....0.01489	21.....0.01521	9.....0.01474	9.....0.01486
10.....0.01541	22.....0.01513	10.....0.01538	10.....0.01510
11.....0.01464	23.....0.01470	11.....0.01525	
12.....0.01514	24.....0.01470	12.....0.01508	

Dementia praecox: Maximum, 0.01542; minimum, 0.01441; average, 0.014910.
Manic-depressive psychoses: Maximum, 0.01538; minimum, 0.01474; average, 0.015060.
Involutional melancholia: Maximum, 0.01549; minimum, 0.01456; average, 0.0150490.

TABLE 6.—*Specific Conductance of Fluids from Various Types of Epilepsy*

Idiopathic	Hereditary	Alcoholic	Endocrine
Case No.	Case No.	Case No.	Case No.
1.....0.01551	1.....0.01484	1.....0.01469	1.....0.01511
2.....0.01473	2.....0.01494	2.....0.01494	2.....0.01513
3.....0.01487	3.....0.01469	3.....0.01486	3.....0.01508
4.....0.01473	4.....0.01483	4.....0.01498	4.....0.01501
5.....0.01470	5.....0.01477	5.....0.01513	5.....0.01515
6.....0.01427	6.....0.01498	6.....0.01473	6.....0.01499
7.....0.01480	7.....0.01490		7.....0.01527
8.....0.01478	8.....0.01491		8.....0.01508
9.....0.01477	9.....0.01482		9.....0.01523
10.....0.01423	10.....0.01476		10.....0.01518
11.....0.01455	11.....0.01490		
12.....0.01481	12.....0.01470		
	13.....0.01477		
	14.....0.01497		

Idiopathic: Maximum, 0.01551; minimum, 0.01455; average, 0.014812+.
Alcoholic: Maximum, 0.01513; minimum, 0.01469; average, 0.014880.
Endocrine: Maximum, 0.01527; minimum, 0.01498; average, 0.015123.

slightly higher than the average normal fluid. If the series were larger, this average might be reduced and be more nearly that of the normal. However, in all cases in which depression was present, it was found that the resistance was higher than in the average normal fluid.

In Tables 6 and 7 are represented the conductance of the fluids from various types of epilepsy. There were 100 fluids in this series. All but thirty of these were classified as to type. All types, except the endocrine, showed lower conductance than normal, while the latter showed slight increase over normal.

TABLE 7.—*Specific Conductance in Epilepsy*

Traumatic		Unclassified Types	
Case No.	Case No.	Case No.	Case No.
1.....0.01532	15.....0.01504	1.....0.01498	16.....0.01484
2.....0.01488	16.....0.01507	2.....0.01488	17.....0.01486
3.....0.01477	17.....0.01527	3.....0.01480	18.....0.01493
4.....0.01494	18.....0.01575	4.....0.01480	19.....0.01486
5.....0.01496	19.....0.01532	5.....0.01494	20.....0.01484
6.....0.01490	20.....0.01500	6.....0.01487	21.....0.01519
7.....0.01488	21.....0.01506	7.....0.01478	22.....0.01521
8.....0.01506	22.....0.01542	8.....0.01487	23.....0.01521
9.....0.01509	23.....0.01528	9.....0.01490	24.....0.01512
10.....0.01498	24.....0.01551	10.....0.01473	25.....0.01509
11.....0.01506	25.....0.01534	11.....0.01506	26.....0.01486
12.....0.01507	26.....0.01519	12.....0.01501	27.....0.01493
13.....0.01505	27.....0.01523	13.....0.01477	28.....0.01507
14.....0.01525	28.....0.01534	14.....0.01490	29.....0.01516
		15.....0.01484	30.....0.01519

Traumatic: Maximum, 0.01534; minimum, 0.01463; average, 0.014899+.
Unclassified types: Maximum, 0.01521; minimum, 0.01473; average, 0.014883+.

TABLE 8.—*Specific Conductance of Fluids in Hemiplegia and All Types of Myelitis*

Hemiplegia		Myelitis, All Types	
Case No.	Case No.	Case No.	Case No.
1.....0.01480	5.....0.01478	1.....0.01468	6.....0.01426
2.....0.01498	6.....0.01549	2.....0.01456	7.....0.01489
3.....0.01517	7.....0.01458	3.....0.01446	8.....0.01436
4.....0.01488	8.....0.01457	4.....0.01512	9.....0.01502
		5.....0.01447	

Hemiplegia: Maximum, 0.01549; minimum, 0.01457; average, 0.014906.
Myelitis: Maximum, 0.01512; minimum, 0.01426; average, 0.014646.

TABLE 9.—*Various Conditions of Nervous System*

Cerebral Arteriosclerosis		Neurasthenia		Lateral Sclerosis		Brain Tumor	
Case No.		Case No.		Case No.		Case No.	
1.....0.01513		1.....0.01491		1.....0.01478		1.....0.01528	
2.....0.01544		2.....0.01461				2.....0.01478	
3.....0.01514						3.....0.01558	
Average.....0.015270		Average.....0.014760				Average.....0.015213	
Senile Dementia		**Paranoid Condition**		**Hydrocephalus**		**Postmeningeal Hemorrhage**	
Case No.		Case No.		Case No.		Case No.	
1.....0.01444		1.....0.01513		1.....0.01452		1.....0.01442	
2.....0.01503				2.....0.01516		2.....0.01364	
3.....0.01514							
Average.....0.01487				Average.....0.01484		Average.....0.014030	
Alcohol Depression		**Delirium**		**Psychoses and Mental Depression**		**Multiple Sclerosis**	
Case No.		Case No.		Case No.		Case No.	
1.....0.01547		1.....0.01530		1.....0.01508		1.....0.01486	
2.....0.01510				2.....0.01522		2.....0.01447	
Average.....0.015285				Average.....0.01519		Average.....0.014665	

Meningo-encephalitis, old.....0.01465

Table 8 represents the results in a series of cases of hemiplegia and myelitis of all types except the syphilitic. The cases of hemiplegia were of several weeks' standing. In both of these conditions, the average conductance was below the normal, this being particularly noticeable in the cases of myelitis.

In Table 9 is represented the resistance in a large number of conditions, in none of which the series was large enough to permit definite conclusions. While some are above the normal, it will be observed that all run very close to the average normal.

Table 10 represents the specific conductance of conditions wherein there is meningeal reaction present as well as a constitutional one, and it is this table that gives the most striking results. In poliomyelitis, the average conductance is considerably less than normal, while in the epidemic type of meningitis it is still lower; it is decidedly decreased in the tuberculous form of meningitis. In the tuberculous type, the chlorids

TABLE 10.—*Acute Infections Involving Meninges*

Poliomyelitis		Epidemic Meningitis		Tuberculous Meningitis			
Case No.		Case No.		Case No.		Case No.	
1	0.01426	1	0.01439	1	0.01268	6	0.01371
2	0.01478	2	0.01382	2	0.01226	7	0.01374
3	0.01471	3	0.01450	3	0.01323	8	0.01313
		4	0.01390	4	0.01317	9	0.01345
				5	0.01374	10	0.01323
Average	0.014583	Average	0.0141025			Average	0.013233+

Normal: Maximum, 0.01549; minimum, 0.01446; average, 0.014953.

in the fluid are markedly decreased, and the conductance bears a distinct relation to this decrease of the chlorid content in the fluid.

SUMMARY AND CONCLUSIONS

Conductivity tests were made on more than 360 spinal fluids obtained from both normal and abnormal conditions of the central nervous system.

It was found that the conductivity depends on the total ionized solids of the fluid, which is composed chiefly of sodium chlorid and other electrolytes.

The protein content of the fluid retards slightly the conductance.

In the various conditions of the central nervous system, the fluids compare closely with the average normal, both in the maximum and minimum and the average resistance measurements. The only striking exception to this is found in conditions with marked meningeal reaction, especially in the tuberculous form of meningitis; this is explained by the very low chlorid content of the fluid in that condition.

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THE MECHANISM OF IMMUNOLOGIC CHANGES IN THE CEREBROSPINAL FLUID*

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The immunology of the cerebrospinal fluid in health and disease has long been a subject of considerable interest and importance, not only from the standpoint of theory and speculation regarding the source and mechanism of immunologic changes, but likewise in relation to natural and acquired resistance of the meninges, brain and cord to infection, and examinations of the fluid for diagnostic purposes.

IMMUNOLOGY OF NORMAL SPINAL FLUID

Before undertaking a discussion of the immunologic changes in the cerebrospinal fluid in disease and the mechanism of their production, it may be advisable first to make a brief survey of the immunology of the normal spinal fluid and the relation this subject bears to infection of the organs of the central nervous system. It has long been known that antibodies commonly found in the blood are not to be detected in the normal fluid. For example, that peculiar constituent of the plasma known as complement or alexin, which plays so important a rôle in lytic immunologic processes, and which is so essential in relation to natural and acquired resistance, is not found in normal cerebrospinal fluid. The opsonins, which are so vitally concerned in the mechanism of the most important single immunologic mechanism of all, namely, phagocytosis, and variable amounts of which are almost always to be found in the blood for pneumococci, streptococci, staphylococci and many other organisms, are usually absent from normal spinal fluid. While the majority of adults have sufficient natural diphtheria antitoxin in their blood to protect against this disease, none of this antibody is to be found in the spinal fluid. The latter is, of course, of little practical importance, because neither the diphtheria bacillus nor its toxin is capable of infecting the meninges, brain or cord, although the latter is believed to affect the cardiac ganglia; but the observation is of interest in connection with tetanus, since the toxin of this disease has a special and important interest in relation to the spinal cord, and the same may be said of the toxins of bacillary dysentery, botulinus and probably some other diseases due principally to exogenous poisons. I have

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repeatedly found traces of natural antitoxin for tetanus in the blood plasma of human beings whose cerebrospinal fluid, even in amounts as high as 5 c.c., showed absolutely no more neutralizing power for tetanus toxin than physiologic sodium chlorid as determined by guinea-pig inoculation tests. Agglutinins and bacteriolysins for typhoid and various other bacilli are likewise usually absent in normal spinal fluid; at least this has been my experience even in the case of persons immunized with typhoid vaccine and showing agglutinins in their blood serum in dilutions as high as 1 : 100.

Therefore it may be stated that the normal spinal fluid is usually devoid of those immunologic principles known to be present in the blood of all or a large majority of human beings. But of what significance are these observations? Does it mean that the organs of the central nervous system are thereby rendered more vulnerable to parasitic attack or less capable of recovery from infection? Are organisms and their toxins spread broadcast throughout the spinal and cerebral subarachnoid space because the cerebrospinal fluid is lacking in these natural principles of resistance? In the case of the diseases due to direct involvement of the meninges, brain and cord by way of the lymphatics, I am inclined to believe that the absence of protective principles in the spinal fluid favors infection. For example, if natural tetanus antitoxin were present in the fluid, I believe that involvement of the anterior horn cells of the spinal cord would be less likely to occur. In other words, it is a demonstrated fact that free tetanus toxin may be found in the spinal fluid in cases of this disease and apparently may be absorbed into the substance of the spinal cord; at least, it is known that tetanus antitoxin injected subthecally is capable of preventing tetanus or dissociating and neutralizing a portion of toxin already involving anterior horn cells, and it is reasonable to assume that both toxin and antitoxin in the fluid are capable of penetrating into the substance of the cord. Likewise, if antibodies for meningococci, pneumococci and streptococci were present in the fluid, I believe that we should more frequently escape the meningitides due to direct extension of these organisms from the mastoid cells, accessory sinuses and lymphatics of the upper respiratory tract. But when organisms are brought to the meninges, brain and cord by the blood, we cannot blame this antibodyless state of the cerebrospinal fluid for the resulting infections. For example, the spinal fluid is in no way to blame for infection with *Spirochaeta pallida,* or for tuberculosis of the meninges or those cases of meningococcus, pneumococcus or influenzal meningitis secondary to bacteremias. The organism may have a selective affinity for these tissues and effectually overcome what may be a considerable resistance on the part of the blood, and invade and infect the meninges, brain and cord without in any manner involving the question of resistance on the part of the spinal fluid, even though

the principles of resistance were present. But organisms brought to the meninges by the blood may gradually work their way through the tissues to the free surface of the subarachnoid and pia mater, and, finding no resistance to their proliferation in the spinal fluid, may be readily distributed through the subarachnoid space of the cord and brain, so that the cerebrospinal fluid may become a carrier and distributor of organisms and toxins rather than a fighter of infection by means of natural immunologic principles. Strictly speaking, therefore, the lack of natural antibodies in the cerebrospinal fluid is of importance in relation to infection only when organisms or their toxins have actually reached the fluid and find there no resistance to their presence or proliferative activities. Possibly this state may bear a relation to infection of the meninges by way of the lymphatics, but I cannot understand how the matter of presence or absence of antibodies in the fluid bears any relation to resistance to those organisms or toxins brought to the meninges, brain or cord by the arterial blood; this includes *Spirochaeta pallida* and most of the other pathogenic agents capable of infecting these tissues, although, as stated, when these incidentally find their way into the spinal fluid, the latter is to be blamed in part for their subsequent distribution throughout the subarachnoid space.

But if the normal cerebrospinal fluid is regarded as a product of secretion by the choroid plexus and selective filtration by the endothelial cells lining the subarachnoid and pia-mater, we should not expect to find natural antibodies in it any more than we may find them in the normal fluid of the joints, pericardium, peritoneum and other serous cavities, as well as in the humors of the eye. I have repeatedly secured sufficient amounts of these fluids during necropsies on human subjects made immediately after death and larger amounts from cattle at abattoirs to make various tests for complement, opsonins, agglutinins and bacteriolysins, and have had uniformly negative results. In other words, just as the normal epithelium of the kidneys and mammary glands hold back certain constituents of the blood, including the natural antibodies, so likewise the endothelium of the serous cavities concerned in the secretion of these normal fluids largely for mechanical functions, including the subarachnoid space, fails to pass many of the soluble constituents of the plasma, including the antibodies. Owing to the great physiologic importance of the brain and cord, our attention is naturally more frequently and intensely focused on the cerebrospinal fluid. I believe the mechanism of its normal production is almost similar to that concerned in the production of lubricating fluids in other serous cavities, but with the difference that the choroid plexus is present as an additional organ for secretion or selective filtration because of the larger amounts of cerebrospinal fluid required for physiologic functions. The cells concerned in its production do not, however, normally or naturally permit

the passage of antibodies in the plasma; why this is so, we do not know, and we cannot help but believe that nature is defective in this particular instance.

IMMUNOLOGY OF SPINAL FLUID IN DISEASE

Are antibodies present in the cerebrospinal fluid in disease, and, if so, by what mechanism are they produced? With the exception of syphilis, our information on these subjects is rather meager, because we do not usually secure spinal fluid for purposes of study and investigation unless there is an indication or possibility of involvement of the central nervous system. According to the result of examinations of spinal fluids from cases of diphtheria, scarlet fever, pneumonia, typhoid fever, etc., which I have been able to make for complement, natural diphtheria antitoxin and various opsonins, bacteriolysins and complement-fixing antibodies, the general statement may be made that acquired antibodies are not to be found in the spinal fluid regardless of their concentration in the blood unless there is some involvement of the meninges. My associates and I have also attempted passively to transfer antibodies from the blood to the spinal fluid in dogs. We were unsuccessful except when the normal inhibitive secretory mechanism of the cerebrospinal fluid was disturbed by intraspinal injections of serum, broth or some such irritant; in other words, the mechanism holding back normal or natural antibodies is likewise capable of doing so when these antibodies are greatly reenforced by the immunizing processes of disease or vaccination. I believe the same is true of the renal epithelium, the endothelium of the large serous cavities and to some extent of the glandular epithelium of the mammary glands. These excretory or secretory cells do not normally pass the antibodies of the blood regardless of their concentration in the plasma, providing the cells are in a normal condition and there is no active or passive hyperemia.

In the presence of vascular changes, however, this selective inhibitory mechanism is disturbed. Thus, in the ascitic fluid of cardiorenal-hepatic disease, there are occasional traces of various blood antibodies, especially the reagin of the Wassermann reaction; likewise there are traces of antibodies in the pleural and pericardial fluids of cardiac decompensation, as well as in the milk during the first few days or weeks of lactation when the glands are especially hyperemic. In other words, transudates in the large serous cavities may contain small amounts of various antibodies probably due primarily to the physical mechanism or transudation of plasma constituents resulting from excessive hyperemia and to a lesser extent from excessive secretion or excretion sufficient to break down selective inhibition. In the sterile cerebrospinal fluid of human beings with acute meningeal congestion, erroneously designated as "serous meningitis" or "meningismus," and developing

during alcoholism, pneumonia, measles and whooping-cough, I have occasionally found natural antisheep hemolysin and traces of complement doubtless carried over into the fluid from the blood as a result of the acute vascular disturbances.

In acute and chronic meningitis one may find in the cerebrospinal fluid traces of complement, antisheep hemolysin and opsonins, but usually in surprisingly small amounts considering the degree of disturbance. In a study of fluids from cases of meningococcus and pneumococcus meningitis, I was so impressed with the frequency with which no complement was present in the fluid that I advise, and frequently practice, the addition of sterile human or guinea-pig serum to the immune serum prior to subthecal injection for the purpose of activating the bacteriolysins and reenforcing the bacteriotropins of the immune serum and thereby enhancing curative activity.

Probably the most marked alteration in the antibody content of the spinal fluid occurs in syphilis. From whence are derived the reagins or antibody-like substances responsible for the Wassermann reaction, the precipitation of colloidal lipoids, gold, mastic, benzoin, etc.? Why is it that the blood of a syphilitic patient may yield a negative blood Wassermann reaction when the spinal fluid may react positively? It is my opinion that the antibody-like substance responsible for complement fixation in the Wassermann test is identical with that causing the precipitation of lipoids in colloidal suspension in the Sachs-Georgi, Vernes, Kahn and hosts of similar tests and reactions described from time to time during the past eighteen years. I also surmise that the same antibody-like substance is responsible for the precipitation of colloidal gold, colloidal mastic, etc., and that it is a reactionary product of the lymphocytes and fixed tissue cells in direct contact with the antigenic substances elaborated by *Spirochaeta pallida;* if this is true, Neisser's term "reagin" would appear to be a particularly appropriate name for this substance, because it does not seem to be a true antibody in the sense of being destructive for *Spirochaeta pallida.* At least my colleagues and I had the Wassermann reaction demonstrated in chancre fluids many days before it was found in the blood, and it is my opinion that the antibody-like substances responsible for all of these reactions is a product of the admiring circle of cells surrounding depots of spirochetes, and that it is possible for it to be produced wherever the parasites are located, including the meninges, brain and cord. If this is true, one may expect to find in the cerebrospinal fluid a large production of the reagin in cases of syphilis of the central nervous system, the amount varying with the degree of infection, being largest in general paralysis because of the numerically heavy infection and smallest in tabes dorsalis because of the sparsity of spirochetes and more limited involvement of meninges

and cord. As would be expected, the blood serum in the majority of cases of neurosyphilis also yields positive Wassermann reactions, because we know that most patients also have syphilitic infection of the cardiovascular or other organs; sometimes, however, the blood Wassermann reaction is negative while the spinal fluid reaction is positive. Whenever this happens, I have surmised that the visceral involvement, as of the myocardium, aorta or other organs, is so slight and latent that detectable amounts of reagin are not being thrown into the blood, while the heavier infection of the meninges, brain or cord produces more reagin in the spinal fluid. Too much emphasis must not be placed on propositions of this kind, because many such instances can be explained on purely technical grounds since we may use from five to ten times more spinal fluid than serum for conducting the Wassermann test. This increases the sensitiveness of the test with spinal fluid because its content of proteins and inorganic salts is so much lower than that of serum that the degree of precipitation of colloidal lipoids with consequent adsorption or fixation of complement is not reduced. Contrary to the usual impression and expectation, there is a limit to the amount of serum that one may employ in the complement-fixation test for securing reactions of the maximum degree of specificity and sensitiveness. It may appear that 0.4 c.c. of serum will give a stronger reaction and detect traces of syphilitic reagin when 0.1 or 0.05 c.c. amounts fail to do so; but curiously enough the inorganic salts or proteins of the serum tend to interfere or to reduce the degree of complement fixation in syphilis, so that a large amount of serum may give a weaker reaction than a smaller amount and may even yield a falsely negative reaction. I know this is the case with my new complement-fixation test for syphilis, and it constitutes the most important single reason for testing all serums in graded and varying amounts instead of in a single amount; at least two different doses should be employed in order to reduce this biologic error to a minimum. With spinal fluid, however, the necessity for using varying amounts in the Wassermann test is not present, and in general terms the larger amounts always yield stronger reactions than smaller amounts. It is a safe general rule that in any method at least from five to ten times more fluid may be used than serum with a consequent increase of sensitiveness. Furthermore, spinal fluid may be used without preliminary heating at 55 C., since complement is not present requiring inactivation; this adds to the sensitiveness of the reactions, as some syphilis reagin is always lost by the process of heating; for this reason I have reduced the period for heating serums from thirty to fifteen minutes at 55 C. in our new test. Finally, the cerebrospinal fluid is less likely to contain natural antisheep hemolysin which may contribute in a small way to an increase of sensitiveness of the Wassermann

reaction, although in general paralysis goodly amounts of this hemolysin and traces of complement may be present in the fluid as detected by the Weil-Kafka reaction

SUMMARY

1. Normal cerebrospinal fluid does not usually contain the natural or normal antibodies to be found in the blood because of a selective inhibitory mechanism of the cells concerned in its secretion or excretion, and in part because the fluid is so frequently renewed.

2. Even when the antibody content of the plasma is greatly increased as a result of immunization by disease or vaccination, antibodies are not usually to be found in the normal spinal fluid.

3. The absence of antibodies in the spinal fluid is of importance in relation to those infections of the meninges by way of the lymphatics, and greatly aids the dissemination of infection throughout the subarachnoid space when organisms or their toxins have reached the fluid.

4. In acute and passive congestion of the meninges with serous exudation and transudation, antibodies from the plasma may be passed into the spinal fluid, but only in small and irregular amounts.

5. In acute and chronic meningitis, traces of antibodies may be found in the cerebrospinal fluid.

6. Under these conditions, antibodies reach the spinal fluid as a result of such physical processes as transudation or exudation of plasma from the blood rather than by any important removal or decrease of the selective inhibitory secretory or excretory mechanism of the choroid plexus or endothelial cells lining the meningeal spaces.

7. It is highly probable that the Wassermann and other antibody-like substances of syphilis are produced in the meninges, brain and cord as reactionary substances of cells in contact with *Spirochaeta pallida*. For this reason the spinal fluid may yield positive Wassermann reactions when the serum reacts negatively; it may also account in part for variations in the serologic reactions of fluid taken at different times and at different levels; but spinal fluid reactions of this kind are more likely to be due to the use of larger amounts, the absence of natural hemolysins and complement, and the fact that the fluid is not heated with consequent reduction in the amount of the complement-fixing reagin.

EMBRYOGENESIS OF HUMAN CEREBROSPINAL FLUID

SOURCES, CIRCULATORY PATHWAYS AND DESTINATION, TOGETHER WITH RELATION TO BLOOD AND LYMPH VASCULAR SYSTEMS *

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The probable source and circulatory pathways of the human cerebrospinal fluid have been ascertained in comparatively recent years, although Magendie [1] published his observations on the character of the fluid just a century ago. The origin of the fluid has yet to be proved absolutely, although the choroid plexus theory seems almost incontrovertible.

During the past ten years, Weed,[2] by splendid experimental work, has cleared up many perplexing points in what might be called the life history of this body fluid, and necessarily I shall quote him extensively. Clinical application of his studies has shown that facts demonstrated in experimental animals are entirely analogous to conditions found in the human being. In no part of the body is physiologic control of anatomic knowledge more necessary than in a study of the cerebrospinal fluid and its pathways. Only those findings can be accepted as final which are supported by experimental evidence of the highest possible quality.

ORIGIN OF CEREBROSPINAL FLUID

To speak of the embryogenesis of a fluid, the adult origin of which still lies somewhat in doubt, is hardly a logical procedure, but a brief review of the facts at hand regarding the activity of the choroid plexus will probably furnish the necessary justification.

Faivre [3] first described the glandular structure of the choroid plexus, and was supported by Luschka's observations a short time later. This marked the abandonment of the earlier theory that the cerebrospinal fluid was elaborated by the leptomeninges. The hypothesis that the choroid plexus elaborates the greater portion of the cerebrospinal fluid has formed the working basis of all subsequent investigations.

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* Read before the Association for Research in Nervous and Mental Diseases, Dec. 29, 1925.

1. Magendie, F.: Paris, 1825.

2. Weed, L. H.: J. M. Res. **31**:93, 1914; Contributions to Embryology No. 14, Publ. No. 225, Carnegie Inst., Washington, 1917, p. 1; Am. J. Anat. **31**:191 (Jan.) 1923.

3. Faivre, J. J.: Thèse de Paris, 1853, No. 142.

Much has been done to demonstrate the presence of intracellular secretion granules in the cells of the plexus and the actual production of the liquid surrounding the cells. Other authors, notably Cappelletti,[4] Pettit and Girard,[5] and Meek,[6] using a combination of pharmacologic and histologic methods, demonstrated increased secretory activity under the influence of muscarin, pilocarpin, etc., while atropin and hyoscyamin diminished it. Definite changes were found in the cells of the plexus following the use of these drugs.

Experimental and pathologic obstructive internal hydrocephalus points definitely toward intraventricular elaboration of the fluid. Cushing's [7] observation of an exudation of clear fluid from a choroid plexus exposed in the course of an exploration; Weed's catheterization of the aqueduct of Sylvius resulting in a sustained flow of fluid; and, finally, Dandy's [8] extirpation of the choroid plexus in an obstructed lateral ventricle preventing the development of an internal hydrocephalus, all lend strong support to the general theory. Weed's studies on the development of the cerebrospinal spaces, add another link to the chain. Weed has also advanced evidence indicating that possibly the perivascular spaces and even the cells lining the ventricles may elaborate a certain amount of fluid into the subarachnoid spaces. This might possibly account for the difference in character of the ventricular and spinal fluid.

His [9] and Kölliker [10] were the first to demonstrate in man the development of the meninges from mesenchyme and the differentiation of the cerebrospinal membranes to form the subarachnoid space. Reford, working in Mall's laboratory, made the only attempt previous to Weed's to solve the problem of development of the cerebrospinal space by the method of injection. Unfortunately, Reford's work was never published. Methods of injection of the subarachnoid space in the adult have, in general, involved the introduction of the foreign solution under considerable pressure. Such a method in the embryo is obviously unpractical because of the extreme delicacy of the embryonic tissues. Consequently, Weed introduced fluids at normal pressure, gradually replacing the cerebrospinal fluid with some foreign isotonic solution.

These experiments were carried out on embryo pigs, whose central nervous system and its coverings develop much as in man. The fluid was introduced through the caudal central canal and withdrawn from a

4. Cappelletti, L.: Arch. ital. de biol. **35**:463, 1900.
5. Pettit, A., and Girard J.: Arch. d'Anat. Mic. **5**:213, 1902.
6. Meek, W. J.: J. Comp. Neurol. & Psychiat. **17**:286, 1907.
7. Cushing, H.: J. M. Res. **31**:1, 1914; Mitt. a. d. Grenzgeb. d. Med. u. Chir. **9**:773, 1902.
8. Dandy, W.: Tr. Am. Surg. Assn. **37**:397, 1919.
9. His, W.: Leipzig, Engelmann, 1865.
10. Kölliker, A.: Ed. 2, Leipzig, Engelmann, 1879.

lateral ventricle. The embryos were kept alive in an incubator for varying periods—usually one hour—thus allowing the spread to become complete. The solution was a 1 per cent. concentration of potassium ferrocyanid and iron-ammonium citrate. Precipitation of Prussian blue granules in situ was effected by fixation with liquor formaldehydi and a small amount of hydrochloric acid.

PATHWAYS OF CEREBROSPINAL FLUID

In a living pig embryo of 9 mm., the ventricles can be fairly well filled without rupture of any element. The solution then spreads to the bulbar region and extends outward into the large fourth ventricle. At this stage, the solution is wholly contained within the medullary canal system—there being no evidence whatever of spread outward from either the third or fourth ventricle. In a 13 mm. embryo, using the replacement method of injection, with the exception of an area of condensation of the fluid on the anterior half of the ventricular roof, there is no difference from the stage preceding, and there is still no indication of a meningeal fluid cushion corresponding to the adult subarachnoid space. From the 14 mm. stage onward, however, the picture gradually changes. In a pig embryo of 14.5 mm., there is for the first time indication of a spread through the roof of the fourth ventricle. Here there is a delicate, fusiform extension of the fluid caudalward from the roof of the fourth ventricle, lying between this point and the skin. At this same stage, the small depression on the roof of the ventricle, which marks the beginning formation of the choroid plexuses, is first noticed. At 18 mm. conditions are much the same, but a new phenomenon is exhibited. The choroid plexus invagination has now divided the roof into two parts, and from these two parts the entire escape of the injection fluid into the pericerebral tissues has taken place. The spread of the fluid is considerably greater than at the last stage, extension taking place in all directions; that is, superiorly, inferiorly and laterally. There is still no evidence of a perispinal spread. Further spread now takes place rapidly, with increase in size of the embryo, and at 21 mm. the fluid can be traced caudalward in the perispinal spaces to the point of injection. In the cephalic region the spread is extensive. The rhombencephalon is completely surrounded, and laterally the Prussian blue is shown as a dense mass in intimate relation to the cranial nerves where they join the brain stem. The spread, therefore, is now almost complete, the only areas not entirely surrounded being the anterior mesencephalon and the cerebral hemispheres. Study of a 26 mm. embryo shows the injection occupying the whole medullary canal system and also completely surrounding the cerebrospinal axis. In addition, there is extension of the granular material laterally along each spinal nerve, extending only so far, however, as the ganglia on the posterior roots. The adult

relationship holds, therefore, at the 26 mm. stage so far as the pathway of the periaxial spaces is concerned, the distribution of the cerebrospinal fluid and the sole communication between the ventricles and the perispinal spaces, the latter fact at variance with the findings of Bichat and Mierzejewsky, but in accordance with the observations of Dandy and Blackfan.[11]

Weed explains this spread largely on the basis of filtration—the fluid going from a point of higher to one of lower pressure. There must, however, be some mechanism whereby passage outward of the normal protein content of the cerebrospinal fluid may take place. This phenomenon may be effected either by a phagocytic property of the cells of the area membranacea of Weed, or else by a process similar to but slower than the normal fluid passage. In replacement experiments in which suspensions of India ink were used neither of these factors could be demonstrated, due doubtless to the size of the carbon granules.

We may now turn to the problem of ascertaining the relationship between the developing choroid plexuses and the extension of fluid into the periaxial spaces. Weed also has investigated this problem, using pig embryos. In the 14 mm. stage there is, as noted, a beginning spread of the ventricular fluid into the periaxial spaces. This occurs practically simultaneously with the first indication in the pig embryo of the choroid plexuses of the fourth ventricle. It would seem, therefore, that there is some relation between the two. In the 18 mm. stage the choroid plexus is well advanced, and at 20 mm. the tufts in the fourth ventricle are marked. Not until the 19 mm. stage, however, is there any indication of the plexus in the other ventricles. A perfectly definite differentiation occurs then at 23 mm., suggesting some relationship to the complete periaxial spread found in embryos of this measurement. With this gradual development of plexuses and the coincident spread of fluid into the pericerebral and periaxial spaces, it seems reasonable to conclude that with the first appearance of the choroid plexuses a more rapid production of cerebrospinal fluid occurs, necessitating the passage of fluid into the periaxial spaces and lending further support to Weed's suggestion in regard to the passage of fluid from a point of higher to one of lower pressure.

Though no evidence was brought forward by Weed to elucidate the interesting problem of the development of the various foramina—in all his experiments histologic examination showed the membranes to be intact throughout and that the spread took place through the differentiated areae membranaceae, superior and inferior—nevertheless, in a consideration of the adult circulation of the fluid we are obliged to accept the existence of the presence of the foramina of Luschka and Magendie.

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11. Dandy, W. E., and Blackfan, K. D.: J. A. M. A. **61**:2216 (Dec. 20) 1913.

The exact mode of escape, however, is still a matter of uncertainty. Whether these foramina are artefacts or whether an actual functioning opening develops in the velum, it is through these three foramina, or at least in the region of the tela choroidea, if through an intact membrane, that the fluid produced in the ventricles passes into the subarachnoid space.

The route of flow of the fluid formed in the lateral ventricles, therefore, is through the foramen of Monro into the third ventricle, by the aqueduct of Sylvius into the fourth ventricle and thence through the foramina into the subarachnoid space. From the cisternal dilatation of the subarachnoid space in the region of the medial cerebellobulbar angle, the fluid gradually seeps downward in the spinal subarachnoid space, but passes with much greater rapidity about the base of the brain, completely around the hypophysis cerebri in the sella turcica, as demonstrated by the author, and thence more slowly over the hemispheres. This movement is probably facilitated by impulses transmitted to it by the vascular system. In the spinal region there is a similar circulation of fluid upward. The speed of flow of this cerebrospinal fluid is governed largely by the density of the delicate, mesh-like trabeculae extending from the outer continuous arachnoid membrane to the pia mater, with which they merge. The arachnoid, trabeculae and pia mater are all covered by flattened, polygonal mesothelial cells. All blood vessels and nerves crossing the subarachnoid space are also covered by the same elements. The meshes referred to above vary in size from fine reticular spaces over the cerebral hemispheres to broader channels in the cerebral sulci and about the spinal cord, and reach their greatest capacity in the cisternal dilatations about the cerebellobulbar angle. Obviously, therefore, the flow of fluid is unobstructed in the wide channels but definitely retarded in the regions of the smaller meshes.

It might be well, too, to call attention to the relation of these mesothelial cells to the subarachnoid and perivascular spaces. The cells of the pia mater turn inward to form an outer wall of such a perivascular channel; the cells of the arachnoid, covering the vessel as it traverses the subarachnoid space, form the inner wall. Thus each blood vessel penetrating the nervous system is surrounded by a cell-enclosed, periadventitial channel which communicates directly with the subarachnoid space. This perivascular channel, where the mesothelial cell cuff ceases, continues inward to connect directly with perineuronal spaces about the nerve cells. These ultimate fluid spaces are only potential in character, but represent an important accessory fluid system of the cerebrospinal axis, affording a direct pathway between nerve cell and subarachnoid space.[12] By a potential space is meant that under normal pressure

12. Weed, L. H.: Physiol. Rev. **2**:171 (April) 1922.

conditions the circulation in these spaces is inactive. To demonstrate the assumed patency it must be possible either to force fluid into the space by increased pressure or to have it drawn in by some influence within the central nervous system. The latter method is to be preferred, and fortunately is available. Weed and McKibben [13] first showed that the normal cerebrospinal fluid pressure in animals could be markedly reduced by the intravenous injection of strongly hypertonic solutions of sodium chlorid. This reduction in pressure resulted from withdrawal of fluid from the arachnoid space and shrinking of the brain itself. Weed used this method to demonstrate the possible circulatory pathways and also the routes of absorption of the fluid. This procedure was also used by the author to prove the existence of a continuation of the subarachnoid space about the hypophysis cerebri.

DESTINATION AND DISTRIBUTION OF SPINAL FLUID

A most important factor in the life history of the cerebrospinal fluid, certainly from a clinical standpoint, is the ultimate destination and distribution of this fluid; that is, its absorption. Numerous conditions cause symptoms referable to increase of intracranial pressure, and this increase is probably in most cases due to a hypersecretion and a diminished absorption—the relative degree varying with different diseases.

The literature regarding absorption is extensive; I shall mention only a few of the leading theories, and give the present status of the problem. Key and Retzius [14] were the first to study the problem, and their monograph still stands unique in the skill of its preparation and the splendid character of its plates. They found the chief pathway of absorption to be by way of the pacchionian granulations into the great dural venous sinuses and in addition with accessory drainage indirectly into the lymphatic system. With the supposed discovery that the pacchionian granulations were absent in higher animals and infants, various authors rejected the view of Key and Retzius and proposed other hypotheses. Mott [15] first suggested the possible passage of fluid through the perivascular channels into the cerebral capillaries in animals on whom ligation of the carotid or vertebral arteries had been done. Dandy and Blackfan felt that absorption was a diffuse process from the entire subarachnoid space, and that the cranial portion was more efficient than the spinal. Cushing [7] suggested a valve-like mechanism for drainage

13. Weed, L. H., and McKibben, P. S.: Am. J. Physiol. **48**:512, 1919.

14. Key and Retzius: Anatomie des Nervensystems und des Bindesgewebe, Stockholm, 1876.

15. Mott, F. W.: Lancet, 1910, Pt. 2, pp. 1 and 79.

into the venous sinuses. The pacchionian granulations have since been shown by Weed to be present in all ages of every species.

Weed's masterly investigations are most convincing. The first step was to effect replacement of the cerebrospinal fluid with a foreign injection solution without in any way changing the normal relationship of the intracranial arterial and venous pressures to the cerebrospinal fluid pressure. These norms had been established by Weed and Hughson.[16] Two types of injection were made—a suspension of carbon granules and a true solution of foreign salts. In the second type the solutions were introduced when the cerebrospinal fluid pressure had been reduced to a point well below zero, and the injection fluid was then maintained at a level never in excess of the established normal for the particular experimental animal. At the end of each experiment the animals were killed and immediately received injections of formaldehyd through the heart and, when the ferrocyanid-citrate mixture had been used, sufficient hydrochloric acid to precipitate the Prussian blue. These granules remain unaltered by the technic of histologic preparation.

In brief, Weed showed the following: In the replacement experiments the precipitation of the Prussian blue was wholly localized within the subarachnoid space, and the nervous tissue was absolutely free from coloration, grossly and microscopically. There was also no penetration of the perivascular spaces. The granules, however, were traced directly into the arachnoid villi, projecting into the basilar dural sinuses, particularly the cavernous. Furthermore, the granules could be seen in process of passage through the mesothelial cells capping the villus and through the endothelial cells of all the dural sinuses. When the hypertonic sodium chlorid solution was used, as in the second type of experiment, a different picture was observed. Here the absorption could be traced through the meninges and cerebral substance for a distance of from 1 to 5 mm.; the perivascular channels and the ependymal lining of the ventricles also showed the injection granules. Nanagas [17] had already shown absorption through the ependymal lining of the ventricles in cases of experimental obstructive hydrocephalus, but neither he nor Weed was able to confirm Foley's [18] observation that resorption took place in the cells of the choroid plexus, a view held by certain European investigators. The author has shown a further pathway of absorption, namely, into the substance of the hypophysis. In experiments similar to the foregoing, granules could be traced into the stroma of the pars buccalis outlining

16. Weed and Hughson: Am. J. Physiol. **58**:53-85, 130, 1921; Hughson, W., Method for Administration of Sodium Chlorid for Headaches, J. A. M. A. **77**:1859 (Dec. 10) 1921; Anat. Rec. **23**:21, 1922; Bull. Johns Hopkins Hosp. **35**:232 (Aug.) 1924.

17. Nanagas, J. C.: Bull. Johns Hopkins Hosp. **32**:381, 1921.

18. Foley, F. E. B.: Arch. Neurol. & Psychiat. **5**:744, 1921.

in many instances the cellular columns of this portion of the gland. This fact suggests a possible intimate relation between the cerebrospinal fluid, blood stream and gland at this point. Clinical support of these observations is afforded by the work of Aycock and Amoss [19] on local specific therapy in poliomyelitis.

With this evidence at hand, the view of various foreign authors that the fluid passes into the cerebral substance through the interstices between the ependymal cells and between the cells of the subependymal spaces (von Monokow [20]) is hardly tenable; nor is the frequent assumption of a relation of the lymph vessels and spaces of the brain and meninges with the lymphatic glands borne out by experimental evidence (Stern,[21], Dahlstrom [22]).

Criticism of pathways established by the use of intravenous injections of hypertonic sodium chlorid cannot as yet be met by definite experimental data, that is, so far as normal use of these channels is concerned. It is common knowledge, that marked changes in cerebrospinal fluid pressure occur in various pathologic states, and it is reasonable to believe that under conditions of increased pressure these accessory means of absorption may function actively and serve much in the manner of the complementary space of the thoracic cavities. Furthermore, there is some evidence to indicate a fluctuation of the normal chlorid content of the blood during and following digestion which could readily effect slight changes in the cerebrospinal fluid pressure. Cushing and Foley [23] have shown reduction of pressures following ingestion of sodium chlorid in considerable quantities, and the author has called attention to the relief of intracranial hypertensive headache following the ingestion of this salt.

In this connection we may consider the passage of substances from the blood stream into the central nervous system and cerebrospinal fluid. Unfortunately few convincing data are available although the matter is one of great clinical importance. Stern and Gautier, among others, have investigated the passage of various substances from the blood stream into the central nervous system and subarachnoid space. They regard the choroid plexus as an apparatus of filtration and purification—a protecting glandular membrane. After the injection into the general circulation, they have sought volatile substances in the cerebrospinal fluid, such as alcohol, acetone and chloroform, and fixed substances

19. Aycock, W. L., and Amoss, H. L.: Bull. Johns Hopkins Hosp. **34**:361 (Nov.) 1923.

20. Von Monokow, C.: Schweiz. Arch. f. Neurol. u. Psychiat. **8**:233, 1921.

21. Stern, L.: Schweiz. Arch. f. Neurol. u. Psychiat. **8**:215, 1921.

22. Dahlstrom, S., and Wideroe, S.: Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:75 (Oct.) 1921.

23. Cushing, H., and Foley, F. E. B.: Proc. Soc. Exper. Biol. & Med. **17**:217, 1920.

such as bromids, iodids, strychnia, lithium, lead, arsenic, mercury and various coloring matters, pigments and acids from the bile and glandular products. These authors have found certain substances circulating and fixed in the central nervous system and others absent—the amounts varying considerably with the different substances used. They are unable to explain these results by any chemical or physical law, but apply to this supposed selective mechanism the name "hemato-encephalic barrier." At present, discussion of this problem is purely speculative. Unless the drug used is one with especial affinity for the nervous system, such as strychnia, there is immediately presented the problem of passage of substances in solution from a point of lower to one of higher pressure. This particular phase of the problem has been considered in the intravenous administration of antisyphilitic drugs after the cerebrospinal fluid pressure has been reduced by the administration of hypertonic sodium chlorid solutions. Many interesting problems await further investigation in this field.

PRESSURE OF CEREBROSPINAL FLUID AND ITS RELATION TO BLOOD VASCULAR SYSTEM

The pressure of the cerebrospinal fluid and its relation to the blood vascular system is another problem of extreme importance which has received much attention. The reports have shown great discrepancies, and in consequence frequent repetitions of the experiments have been made. To note a few: Leonard Hill [24] believed that normal pressures in experimental animals might vary from 0 to 50 mm. of mercury; Dixon and Halliburton,[25] 40 to 70 mm. of Ringer's solution; Becht, 112 mm. of physiologic sodium chlorid; Foley and Putnam,[26] 127 mm., and more recently Weed and Hughson [14] have reported an average of 119 mm. of Ringer's solution. In one of their typical experiments under ether anesthesia, fluctuations in pressure over a two hour period were but 11 mm. It is safe to say that these later observations are more correct and that marked fluctuations in pressure during the experimental period may be regarded as an index of improper technic. Accepting the Monro-Kellie doctrine, which has been subjected to experimental proof by Weed and Hughson, the hypothesis stated by Weed and McKibben,[27] that "the cranial cavity is relatively fixed in volume and is completely filled by brain, cerebrospinal fluid and blood; variations in any one of these three elements may occur, compensation being afforded by altera-

24. Hill, Leonard: London, 1896.
25. Dixon, W. E., and Halliburton, W. D.: J. Physiol. **48**:128, 1914.
26. Foley, F. E. B., and Putnam, T. J.: Am. J. Physiol. **53**:464, 1920.
27. Weed, L. H., and McKibben, P. S.: Am. J. Physiol. **48**:512, 1919.

tion in the volume of one or both of the remaining elements," affords a satisfactory working basis for experimental observations.

Leonard Hill believed that intracranial venous pressure and intracranial pressure were identical, and this view was held generally until Dixon and Halliburton [25] demonstrated "independent changes in pressure occurring as the result of the secretory activity;" but they believed that intracranial venous pressure was higher than that of the cerebrospinal fluid. Becht [28] confirmed this view of independence of pressure while indicating an inconstant relation between the two. All of these observers took their readings of venous pressure from the torcular herophili. This method is defective, as indicated by the wide divergence of the pressure readings. Using a much simpler method, Weed and Hughson were able to show that in practically every case the cerebrospinal fluid pressure was definitely above (5-50 mm.) that of the sagittal sinus. They agreed with Dixon and Halliburton and Becht that alterations in intracranial venous pressure caused like alterations in the fluid pressure, but in lesser degree. The reverse also held true. This pressure relation doubtless plays a large part in the passage of fluid from the subarachnoid space into the dural sinuses, and in addition affords a ready explanation of Wegefarth's [29] experiments. He showed that experimental communication between subarachnoid space and superior sagittal sinus remained patent without hemorrhage into the meningeal cavities for at least four days. Removal of cerebrospinal fluid in these animals, however, resulted in immediate intrameningeal hemorrhage. This could only be possible if the fluid pressure were greater than that in the sinuses.

Weed and Hughson also studied intracranial venous and arterial pressure when the cerebrospinal fluid pressure had been reduced to below zero by intravenous injections of hypertonic sodium chlorid solution. Except for a momentary change in the arterial and venous levels during the period of injection, these pressures are thereafter practically unaffected, while the cerebrospinal fluid pressure falls to its extreme low level and gradually returns to normal after the blood has regained its proper tonicity.

Referring to Reford's work, Sabin,[30] in 1914, makes the following statement: "The arachnoid space has as definite a form as the coelom and it never connects with the lymphatics." This opinion is in marked contrast to that held by various European investigators. Von Monakow speaks of "the lymph vessels of the meninges," indicating thereby a direct intracranial connection with the lymph glandular apparatus. And

28. Becht, F. C.: Am. J. Physiol. **51**:1, 1920.

29. Wegefarth, P.: J. Med. Res. **31**:149, 1914.

30. Sabin, F. R.: Manual of Human Embryology, Keibel and Mall, Philadelphia, 1912, Vol. 11, p. 709.

Stern, though recognizing that the great majority of anatomists deny the existence in the nervous tissues of the cerebrospinal axis of channeled vessels analogous to the lymphatics, seems to place considerable emphasis on the subarachnoid communication with the peripheral lymphatic system by the lymphatic slits of the spinal nerves (described by Finel and Nageotte).

Injection experiments by practically all investigators have shown the presence of the injection mass in the lymph glandular system. Key and Retzius, Quincke,[31] Leonard Hill, Ziegler,[32] Spina,[33] Cushing, Dandy and Blackfan and others mention it, but in almost every instance the appearance of the dyes in the lymphatics is considerably delayed—from one-half to one hour after the injection has been made. This immediately raises the question as to whether this appearance in the lymphatics is direct, or indirect through the blood stream. Weed states that "it seems fair to assume that the absorption of the cerebrospinal fluid is a twofold process, being chiefly a rapid drainage into the great dural sinuses and in small part a slow indirect escape into the true lymphatic vessels."

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31. Quincke, H.: Arch. f. Anat. u. Physiol., 1872, p. 153.
32. Ziegler, P.: Arch. f. Klin. Chir. **53**:75, 1896.
33. Spina, A.: Arch. f. d. ges. Physiol. **83**:120, 415, 1900-1901.

CEREBROSPINAL FLUID PRESSURE

EFFECTS OF SOLUTIONS OF DIFFERENT CONCENTRATIONS *

W. LLOYD AYCOCK, M.D.

BOSTON

Wherefore, in order to form a just notion of the body of man, it ought to be considered as a hydraulic machine contrived with the most exquisite art, in which there are numberless tubes properly adjusted and disposed for the conveyance of fluids of different kinds. Of these the principal is the blood, from which are derived the several humors subservient to the various uses and purposes of life; and in particular that subtile and remarkably elastic fluid, generated in the brain, and known by the name of animal spirits, the instrument of sense and motion; which functions it never could be capable of executing, were it not contained in proper organs. For this purpose the Almighty Creator has formed two sorts of fibres, the fleshy and the nervous, as receptacles for this active principle; and each sort of these is partly interwoven in the membranes of the body, and partly collected into bundles or cords, and attached to the limbs, for performing their motions with the assistance of the bones.

Thus Richard Mead,[1] in 1751, spoke of the central nervous system. In the light of modern knowledge, it may still be said that it possesses certain hydrostatic properties.

There are two distinct components of the cerebrospinal fluid to be considered: that portion which is elaborated from the choroid plexus and that which is derived from the capillary bed of the central nervous tissue.[2]

FUNCTION OF THE FLUID ELABORATED BY THE CHOROID PLEXUS

The bony container of the central nervous organs is of relatively fixed capacity and is completely filled with central nervous organs, blood and cerebrospinal fluid. Variation in the volume of any of these elements may occur, compensation being afforded by alteration in the volume of one or both of the remaining elements.[3] This compensatory function is probably the chief one of the choroid plexus and the fluid which it elaborates. Other functions of this fluid are in part to support and decrease the weight of the fragile and unsuspended brain, to reduce

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* Read before the Association for Research in Nervous and Mental Diseases, Dec. 29, 1924.

1. Mead, Richard: Medical Precepts and Cautions, Dublin, 1751.
2. Weed, L. H.: J. Med. Res. **26**:93, 1914.
3. Weed, L. H., and Hughson, Walter: Am. J. Physiol. **58**:85, 1921.

and distribute the force of impacts to which the central nervous organs are subjected and to provide a lubricant between the cranial and spinal walls and their slightly movable contained organs.[4]

FUNCTION OF THE FLUID FROM THE CAPILLARIES OF THE CENTRAL NERVOUS TISSUE

In principle, the fluid circulation within the nervous tissue is analogous to that of other tissues. With reference to the parenchymal cell the system is composed of three elements: the afferent arterial blood supply, the efferent venous outflow and the accessory fluid system which in function is comparable to the lymphatic of other tissues. There is still considerable uncertainty regarding the mechanism of this system. According to a number of observers, the perivascular system is continuous with a pericellular space, and there is through this channel an uninterrupted exchange of fluid between the parenchymal cell and the perivascular space.[5] The outer wall of the perivascular space is an invagination of the pia-mater, which is brought into the nervous substance by the development of blood vessels.[6] From an embryogenic point of view, it is perhaps difficult to explain the presence of ganglion cells within a space which is described as a continuation of the mesodermally lined perivascular space.

What seems to be a more tenable conception of this system is that the neuroglia is the medium of exchange between the perivascular space and the nerve cell. This is at first suggested by the sucker or footlike processes of neuroglia cells which rest on the walls of perivascular channels and by the fact that where nervous elements disintegrate the proliferating glia envelops broken down particles and phagocytizes them; a portion is resorbed, and a portion is carried away in the protoplasmic pathways of the glial reticulum, and in this manner reaches the perivascular limiting membrane and is pushed through this into the perivascular channel.[7]

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4. Dercum, F. X.: Functions of Cerebrospinal Fluid with Special Consideration of Spinal Drainage and of Intraspinal Injections of Arsphenamized Serum, Arch. Neurol. & Psychiat. **3**:230 (March) 1920.

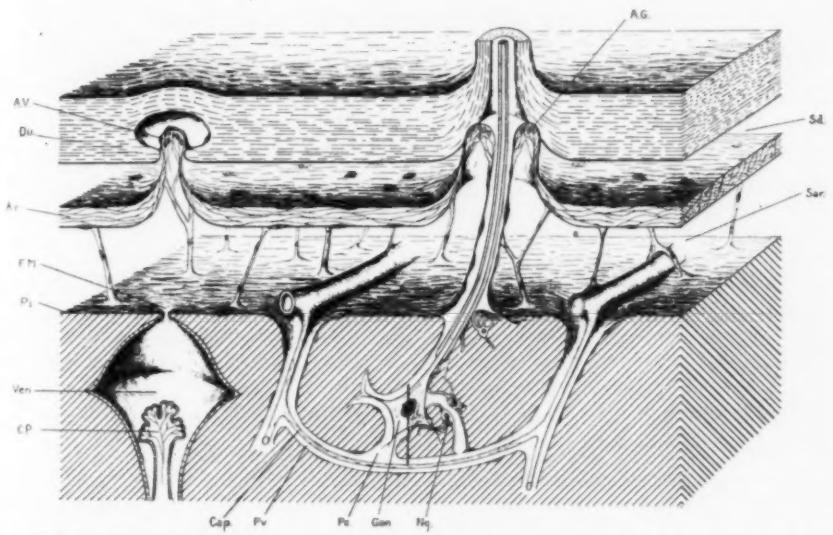
5. His, W.: Ueber ein perivasculares Canalsystem in den nervosen Centralorganen, Engelmann, Leipzig, 1865. Mott, F. W.: The Oliver-Sharpy Lectures on the Cerebrospinal Fluid, Lancet **2**:1 (July 2 and 9) 1910.

6. Schröder, Paul: Introduction to the Histology and Histopathology of the Nervous System, 1923.

7. Kappers, C. U. Ariëns: Vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen, **1**, 1920. Cajal, S. R.: Trabados del laboratorio de investigaciones biologicas **2**:101, 1903; **6**:123, 1909. De Castro, Fernando: Ibid. **108**:1, 1920. Havet, J.: Ibid. **14**:35, 1918.

RELATION OF FLUID CIRCULATION TO LESIONS OF THE NERVOUS PARENCHYMA

In certain diseases of the central nervous system, for example acute anterior poliomyelitis, there is evidence that the primary lesions are those of the interstitial tissue and that the secondary nerve cell injury is the result of failure of the blood or accessory circulation, the immediate cause of the cell damage being lack of nutritive fluid, accumulation of catabolic products or the mechanical effects of edema. To combat these effects, methods are to be sought to increase the passage of nutritive



Schematic representation of the central nervous system, with reference to the circulation of the cerebrospinal fluid. *C. P.* indicates the choroid plexus; *Ven.*, ventricles; *Pi.*, pia; *F. M.*, foramen of Magendie; *Ar.*, arachnoid; *Du.*, dura; *A. V.*, arachnoid villus; *A. G.*, arachnoid granulation; *S. D.*, subdural space; *Sar.*, subarachnoid space; *Ng.*, neuroglia; *Gan.*, ganglion cell; *Pc.*, pericellular space; *Pv.*, perivascular space; *Cap.*, capillary.

substances to the cell, to facilitate removal of its waste products or to reduce edema. In addition, specific medication should be carried to the site of the lesion responsible for the cell damage. Recent developments in the use of salt solutions different concentrations have opened new avenues of approach to these problems.

The pressure of cerebrospinal fluid normally bears a certain relation to the pressures of the blood vascular system and undergoes changes corresponding to changes produced in the blood vascular pressures. In 1919, Weed and McKibben [8] produced marked alterations in cerebrospinal fluid pressure which were independent of changes in blood vas-

8. Weed, L. H., and McKibben, P. S.: Am. J. Physiol. **48**:512, 1919.

cular pressures. The intravenous administration of strongly hypertonic solutions lowered cerebrospinal fluid pressure to an extreme degree. Hypotonic solutions caused a prolonged rise, while isotonic solutions produced only a temporary rise corresponding to the increase in vascular pressures resulting from the intravenous injection.

That the effects of hypotonic and hypertonic solutions on cerebrospinal fluid pressure are due to alterations in the osmotic relations between the blood and the central nervous tissue fluids, is shown by changes in the volume of the central nervous tissue and in the perivascular currents.[9]

These findings have been confirmed repeatedly and have led to clinical application of the phenomena. Reduction of hernia and of edema of the brain and the prevention of leakage of cerebrospinal fluid have been accomplished. The increased passage of substances from the blood to the cerebrospinal spaces is as yet an almost unexplored possibility. The aspiration of suitable remedies from the subarachnoid space into the nervous organs is an important field in the treatment of their diseases.[10]

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9. Weed, L. H., and Hughson, Walter S.: Am. J. Physiol. **58**:53, 1921.

10. Cushing and Foley: Proc. Soc. Exper. Biol. & Med. **17**:217, 1920. Foley and Putnam: Am. J. Physiol. **53**:464, 1920. Sachs and Malone, Am. J. Physiol. **55**:277, 1921. Sachs and Belcher: J. A. M. A. **75**:667, 1920. Ebaugh and Stevenson, Bull. Johns Hopkins Hosp. **31**:440, 1920. Foley: Surg., Gynec. & Obst. **33**:126, 1921. Hughson: J. A. M. A. **77**:1859, 1921. Aycock and Amoss: Bull. Johns Hopkins Hosp. **34**:361, 1923.

Abstracts from Current Literature

THERAPEUTIC VALUE OF HYPNOTISM. ALEXANDER PILCZ, Wien. klin. Wchnschr. **38**:280 (March) 1925.

It is a well-known and disconcerting fact that magnetic healers enjoy large practices. A sadder fact, however, is that these fakirs often produce therapeutic effects on persons who have heretofore been unsuccessfully treated by younger medical men. But the saddest fact of all is that the medical men are themselves to blame for this situation. Trained in the atmosphere of pathologic anatomy, experimental pathology, bacteriology, etc., some physicians are inclined to concern themselves only with the disease of man, completely overlooking the sick man, and entirely underestimating the value of simple psychology. A diagnosis of hysteria with the statement, "that is merely imagination," does not satisfy the patient. He all too often will go away offended and uncured, and fall into the hands of quacks.

The author does not wish to discuss psychotherapy nor to go into the subject of hysteria, he merely wishes to say a word regarding the character and practicability of hypnotism, since this chapter of medicine is treated more or less as a step-child in the official realm of neurology and psychiatry.

For example: Two people are seated at a restaurant table. Everything is very clean, and there is absolutely nothing wrong with the food. The remark is overheard, "Rancid grease was used in preparing this meal." *A* cannot find anything wrong. *B*, on the other hand, insists that he can detect a rancid taste in the food, and sends his meal back. *A* is convinced in his own mind *B* is what we call suggestible. The mere suggestion that there is something wrong is sufficient to call forth the corresponding sensory perception. A suggestible person is one who readily imagines things and is very easily talked into things; he is easily disposed to phantasy and too little disposed to discrimination; that is, he is not capable of thinking for himself.

Every person is suggestible to a certain extent. The degree of readiness to respond to suggestion varies not only in persons, but in each person. In this connection the following conditions are of significance: The personality from which the suggestion emanates (one person can make an impression, inspire confidence, etc.; another cannot); further, the emotional attitude at the time (fear, anxiety, worry, grief, etc.).

We speak of verbal suggestion or suggestion in the waking state in contradistinction to hypnotic suggestion—suggestion in hypnotic sleep. It cannot be too strongly emphasized that there does not exist a sharp line separating waking and hypnotic suggestion, but at most there exists a gradual difference in the sense that in the latter many suggestions may be successful that would have no effect by mere verbal suggestion. For this gradation there are several reasons: first, there are people who are easily hypnotized, naturally suggestible; second, the readiness to respond to suggestion is increased by the technic of hypnotism.

The hypnotizer employs artifices which in a physiologic manner cause a sleepy, tired feeling—the staring at a bright object, gentle stroking over the eyebrows, etc. Then the verbal suggestion, in a lowered tone of voice, "You are getting sleepy—your eyes are closing—breathe slowly—your eyes are locking—you are asleep, etc." The fact that the person being hypnotized actually

experiences these feelings, that he can hardly keep awake and that what the hypnotizer has commanded actually takes place, heightens his suggestibility—his eyes are about to close and the hypnotizer merely presses lightly on the upper lids, and under the influence of this strange will, the hypnotized person loses all sense of judgment, and the floor is leveled for suggestion and his phantasy world.

The hypnotic sleep has but a superficial resemblance to the natural sleep or sleep produced by narcotics. The hypnotized person does not sleep, but believes he sleeps, believes he must sleep, and plays his part.

Who can hypnotize, and who can be hypnotized? Any one can hypnotize who has the necessary authority and who has the power of impressing or imposing his personality on another. Any one can be hypnotized who believes he can be hypnotized, who is willing to push his own judgment to the background, and who may readily be persuaded and is imaginative. This does not necessarily indicate any special "nervousness" or "weakness of will," but more likely a weakness of the discriminating capabilities.

Since we have seen the similarity between verbal suggestion and hypnotism, we can more readily understand the so-called phenomena of post-hypnotic suggestion in which the suggestion made during the hypnotic sleep is not realized until the appointed time after awakening, and therefore in the waking consciousness of the person being experimented on. These post-hypnotic suggestions play the greatest part in the application of hypnotism as a therapeutic measure.

The physician who employs hypnotic suggestions for therapeutic purposes should thoroughly consider the following points at each sitting:

1. He should never hypnotize without the presence of witnesses. This is especially important with women patients, on account of the danger of being accused of unethical methods.

2. Before awakening a patient, the physician should assure the patient that he will awaken easily, and that there will be no after-effect as headache and the like.

3. The physician should assure each patient that in the future no one but the physician will be able to hypnotize him.

The awakening from hypnotic sleep is also brought about by suggestion. The simple suggestion, "When I have counted to three you will awake" is usually sufficient to cause the patient to awaken.

The possibilities of relief through hypnotism may be looked for in the diseases the manifestations of which are brought about in a suggestive manner and really rest on suggestion. The principal domain for hypnotic cures is and will remain, therefore, in the large group of hysterical disturbances, such as paralyses, cramps, contractions, tremor, blindness, etc. Of course, physiotherapeutic measures, verbal suggestions in any form, medication, etc., may bring about cures, but as has been said before, hypnotism and posthypnotic suggestions, as compared with wake suggestions, may be of increased benefit when other measures fail. Hypnotism may also be of value in the various functional disturbances brought about by sexual conflicts, above all psychic impotence, in many cases of sexual perversion, etc. Less gratifying are the results obtained in the compulsion ideas in the endogenous depressions of manic-depressive psychosis. Too little is known of the benefits which may be derived by hypnotism in organic affections so far as they influence subjective complaints. The most variegated paresthesias and pains, even though they

are not "imagined," are much more amenable to suggestion than the practical physician is wont to believe. We need but recall the painless deliveries in the hypnotic "dämmerzustande" long since reported by Kogerer before the Society of Vienna.

It cannot be denied that among physicians (usually the best and most respectable) there exists a certain repulsion toward attempts to cure by hypnotism; the feeling that they do not wish to be looked on as charlatans. This feeling is praiseworthy but not justifiable. Hypnotism when indicated and within bounds is a means of treating the sick man, and in the hands of a conscientious physician is not only harmless, but good results may be obtained which could not be obtained by other therapeutic means. The physician is expected to help—this is his most noble task. If he renounces the mighty help offered through the medium of suggestion, he misses a great deal that an unscrupulous colleague or a quack may see, and he runs the risk of driving many patients to fakirs and quacks who better understand the human mind. He thereby injures the patient in health and morals, but on the other hand also injures his own medical standing.

MOERSCH, Rochester, Minn.

INJURY OF SPINAL CORD BY ARSPHENAMIN MEDICATION. MITSUHISA OSEKI, Arb. a. d. neurol. Inst. **25**:269, 1924.

Injury to the nervous system by arsphenamin is ascribed to various causes. While some look on it as a severe toxic effect of the arsenic, others are inclined to view it as the expression of an intoxication caused by a rapid dissemination of spirochetes. The author describes a case of a woman, aged 29, who acquired syphilis in 1909, developed a rectal stricture in 1910, was treated with mercury, and on March 4, 1914, with arsphenamin, the dose undetermined. On March 5, 1914, she developed paraplegia, retention of urine, paresthesias and later a marked paralysis. Pneumonia set in, and the patient died on March 15. Necropsy showed infection of the conus of a specific nature and pneumonia. There was an enlarged thymus, polypi in the bladder, moderate meningeal inflammation, thickening of the aorta and possibly hemorrhages in the medulla.

Histologic examination of the conus terminalis showed a thickening of the pia, perivascular infiltration of a lymphoid nature, and an infiltration of the gray matter, particularly of the anterior horns, with numerous thick-walled blood vessels which showed many round cells in their sheaths. The central canal was surrounded by many blood vessels filled with blood. The sparing of the white matter and the involvement of the anterior horns was of particular interest. Nissl stain showed neuronophagia of the ganglion cells; some cells showed chromatolysis and dissolution. The small cells showed a similar picture. In all, however, the cell injury was not widespread, though the picture was typical of poliomyelitis. Sections taken above the conus terminalis on first sight showed a typical picture of poliomyelitis, especially of one side, the white substance being spared. The meninges were moderately thickened. The majority of the cells showed swelling and severe injury to the nucleus, and gitter cells were numerous; some showed neuronophagia. Similar pictures were found in the sections from the lumbar region, with necrotic areas in each anterior horn. The same was true of the dorsal portion of the cord. Here, however, the process was less marked, with only incipient foci and relatively intact anterior horns. The infiltration was increased, however, about Clarke's columns, and the pia showed lymphocytic infiltration. In the upper dorsal segments there was a necrotic area on one side, while in the

other parts, the inflammatory process was predominant. The medulla showed some infiltration of the pia. The ganglion cells of the nuclei were completely intact, but there was perivascular infiltration in the region of the hypoglossus nucleus. The pia was moderately infiltrated over the hemispheres.

In summarizing, the author states: "On the one hand we have a severe malacia, and on the other hand, an inflammatory process. It is of interest to note that where the malacia is most prominent, the inflammatory process is recessive, and where the malacia is not prominent, the inflammation is outspoken, especially in the meninges." He does not believe that the inflammatory process is typical of syphilis, but more closely resembles that of poliomyelitis. "One can look upon the process as a malacic form of myelitis."

The author asks whether one can find evidence in the literature of a combined malacia and myelitis not on a syphilitic basis and not on the basis of a previously diseased nervous system, but resulting from one injection of arsphenamin.

Juliusberg and Oppenheim observed a case similar to that of the author clinically. No necropsy was performed. In this case a spastic spinal paralysis set in three days after an injection of arsphenamin. No previous spinal disease was noticed, and the injury was presumably due to the arsphenamin. Westphal reports a case of tabes and spinal syphilitic meningitis in a woman aged 33, in whom, following an injection of 0.4 gm. of arsphenamin dyspnea and death followed. Necropsy revealed tabes and syphilitic meningitis, especially in the cervical and upper dorsal segments. In the third and fourth cervical segments there was an anterior root degeneration which was caused by edema, and which Westphal thought was the cause of the death.

Hoffman describes a case of injury to the spinal cord after the injection of arsphenamin. In this case there was a gumma of the cord; a total hemiplegia followed an injection of arsphenamin. Other authors (Kleinberger, Ullmann and Lewy) described thrombosis of the vessels as found in the author's case, the cause being arsenic intoxication.

Newmark describes a case similar to that of the author. A patient aged 23 received 0.3 gm. arsphenamin, and two days later evidences of weakness in the lower extremities and of vesical disturbance developed. This progressed to a complete paralysis in twenty-four hours, together with disturbance in sensation below the umbilicus. After another injection of 0.6 gm. of arsphenamin, signs of a dorsal transverse myelitis appeared; the patient gradually became worse, and died. Necropsy revealed endarteritis with perivascular infiltration of the vessels. Spiethof, who gave a youth, aged 19, two injections of arsphenamin of 0.5 gm. each, observed meningeal symptoms two days later. Only edema of the cord was present. Wolf and Mulzer report the case of a woman, aged 27, who developed a transverse myelitis following the injection of neo-arsphenamin. She died in a short time. The cord showed necrotic areas, as in the author's case, and inflammation about the vessels as a reaction to the injury.

Fleischmann reports a case of a man, aged 35, who received two injections of 0.5 gm. of arsphenamin. About thirteen days after the second injection, paresis of the lower extremities occurred followed by paresthesia. This progressed, and death occurred in fourteen days, due to Landry's paralysis. Necropsy showed normal vessels and severe acute degeneration of the cells of the anterior horns. Jacob reports a case in which death followed the injection of arsphenamin. Necropsy showed tabes, syphilitic endarteritis and a thickened spinal pia. Kerl reports two cases of injury to the cord after the

injection of arsphenamin. In one case, the symptoms appeared in three weeks and in the other eleven days after the injection. One case showed an acute myelitis, and the other only cerebral edema.

Socin reports a case of malacia in the cord after an injection of arsphenamin. Stühmer observed acute paraplegia developing after the injection of arsphenamin. Mayer observed a similar case in a patient aged 17.

ALPERS, Philadelphia.

SUPPOSED SYMPATHETIC INNERVATION OF THE STRIATED MUSCLES. F. BOTTAZZI, Arch. di Sc. Biol. **6**, 1-2, 114 (Sept.) 1924.

The author refers to the experimental works of the Japanese physiologists (Ken-kuré Tetsushiro Shinosaki, Michio Kishimoto, Michisaburo Sato, Nobuo Hoshino, Yoshinobu Tsukiji) and those by Spiegel, Terni, Muller and others, on the tonic function of the sarcoplasm and its relation to the nervous system. Such relation, which is based on the hypothesis that the accessory amyelinic nerve fibers ending in the muscle fibers belong to the autonomic nervous system, has gradually led to the admission of an autonomic innervation of the striated muscles.

For the purpose of giving an experimental test to this hypothesis, Bottazzi has chosen the diaphragm from the other muscles, because it possesses particular tonic properties, and because its sympathetic supply can be easily traced to the inferior cervical ganglion, the stellate ganglion, the first thoracic ganglion and the semilunar ganglion.

If a sympathetic tonic innervation of the striated muscle exists, this must be demonstrable by an increase in the muscle tone caused by electric stimulation of all the sympathetic structures from which possibly the fibers for the diaphragm originate. This effect will be more conspicuous than that of the diminution of the muscle tone caused by the destruction of the sympathetic ganglia and fibers. Electric stimulation was therefore applied to the great splanchnic and celiac ganglia, to the phrenic nerve and its spinal roots, to the third, fourth, fifth, sixth and seventh cervical nerves at different periods after neurotomy, with the following results:

In animals in whom the motor innervation of the diaphragm had been destroyed from a week to about two months before, stimulation applied to all such structures which might possess sympathetic fibers for the diaphragm did not produce the slightest trace of tonic contraction in the diaphragmatic muscle. The author observes that if the Japanese authors are correct in that there exists a certain compensation between the motor innervation and the tonic innervation of the diaphragm, so that when the first is lacking the latter becomes more intense, his animals should have demonstrated the existence of the supposed tonic innervation, because in some of them in which the motor innervation had been destroyed long before, the sympathetic tonic innervation should have been more evident.

In cases in which he could demonstrate the existence of diaphragmatic reflexes provoked by means of stimulation of the solar plexus and of the splanchnic plexus, he found inhibitions.

The author takes exception to the assumption of the Japanese authors that the trophism of the diaphragmatic muscle depends not so much on its spinal motor innervation as on the sympathetic innervation. In at least two cases (dogs that were kept alive long after the destruction of the spinal motor fibers of the phrenic nerve) the author found the diaphragm on the side of the lesion

seriously altered, in spite of the fact that its sympathetic innervation had been completely spared and the normal motor function of the opposite intact diaphragmatic portion had supplied a kind of rhythmic massage to the injured portion. In the two aforesaid cases the diaphragm was in one case slightly excitable directly by faradic stimulation, in the other case little or not at all excitable. The diaphragm in the more serious of the two cases appeared pale, yellowish, and was reduced to a thin transparent lamina, as shown in a photograph made in situ.

Judging from these results, the author concludes that a tonic innervation of the diaphragm, and therefore probably of the striated muscles in general, does not exist.

This research work is in accord with the recent findings by Kanavel, Pollock and Davis, obtained by other methods. It suggests moderation and less enthusiasm in surgical interventions on the sympathetic advocated recently to relieve paralytic and spasmodic conditions.

NACCARATI, New York.

THE MEDICAL SERVICE OF THE NEW YORK STATE HOSPITALS. G. H. KIRBY, W. L. RUSSELL and J. R. ROSS, State Hosp. Quart. **10**:3 (Nov.) 1924.

The committee on medical service of the New York state hospitals, after a tour of inspection, report in detail their findings, and offer suggestions and recommendations. They find that the conditions under which the medical work is carried on are less satisfactory than in former years as the result of overcrowding, a smaller ratio of physicians and attendants to patients, and additional work incurred by staff meetings, training school lectures and special procedures. They point out that if it were not for the marked increase in the number of patients on parole, the overcrowding would be much worse than it is. The committee considers that the internal medical organization and equipment have not developed to correspond with recent developments in psychiatry and with the growing need for closer affiliation with other branches of medicine. Except for the appointment of clinical directors in some of the hospitals, no new principles of medical staff organization have been introduced in twenty years.

Objection is made to the operation of a reception service as part of a large heterogeneous service, and particularly to the transfer of patients with chronic conditions to wards in which new patients are received. In some hospitals new patients were passed through the reception service too rapidly, many of them being plainly in need of mental or physical treatment. The committee believes that the assignment of new patients for study by physicians in charge of chronic services is bad, as these physicians do not feel that they are responsible for the treatment or proper examination of the patients. It is suggested that a better method would be to give physicians in charge of services devoted to chronic cases access to new patients but to place the responsibility for the initial working up and care of these patients on the physician in charge of the reception service. In the opinion of the committee, the "central office" is responsible for much waste of time, keeps the physicians away from their patients and interferes with systematic clinical work, because it necessitates traveling back and forth many times a day to sign reports, look up records, dictate notes, etc. It is suggested that the term "chronic" as applied to a service or group of patients be dropped and replaced by the phrase "continued treatment group." The committee find that the distinction between acute and chronic services is not based on an understanding of the cases that require

prolonged care. Examples are cited to show that physicians had made notes on almost 300 cases in a week, and one physician had made sixty-three notes in one day.

Among the final recommendations of the committee are: revision of the provisions for reception, intensive study and treatment in all new cases; establishment of a diagnostic clinic; the appointment of one or more additional physicians for parole and outpatient work; the appointment of visiting specialists; the appointment of a clinical director at all hospitals; an annual report by each superintendent similar to that of this committee, and a system of standardization by means of which the best features of each hospital can be incorporated in all.

HOWARD, Milwaukee.

THE NATURE OF THE IMPULSE THAT AFFECTS THE CRISTA AMPULLARIS OF THE SEMICIRCULAR CANALS. A PRELIMINARY REPORT. F. J. NOVAK, JR., Arch. Otolaryngol. **1**:213 (Feb.) 1925.

Novak, realizing that the theory of endolymph movement and the theory of hydrostatic pressure as the cause of labyrinthine stimulation have not been proved, has undertaken some experiments with a model, which I shall quote in full:

"In order to test out this theory that the impulse is an electrical one, I have carried out certain experiments."

"First series.—A glass model of a semicircular canal was constructed. Two small wires, one from each end of the canal were connected with a micro-milammeter. . . . The canal was filled with water in which a small amount of sodium chloride was dissolved. One end of each of the two wires was immersed in this solution. The other two ends were connected with the milammeter. Under these conditions observation of the milammeter showed that there was no electrical current within this circuit."

"When the ampullar end of the canal was heated, the indicator on the milammeter soon showed the presence of an electrical current flowing in one direction. When the ampullar end was chilled, an electrical current flowing in the opposite direction was observed."

"Second series.—Another model (large scale) of a semicircular canal was constructed, into the ampullar end of which a fine platinum wire was sealed, the end of the wire projecting into the ampulla. In a similar way another wire was sealed into the other end of the canal. The canal was filled with a 1 per cent. sodium chloride solution. These two wires were again connected with the milammeter which showed no deflection of the indicator. The wires were then disconnected —— and the model was mounted horizontally in a slow centrifuge and rotated. At the end of rotation the wires were again connected with the milammeter, which immediately indicated the presence of an electrical current in the solution. Rotation of the model in a direction opposite to the first showed on the milammeter a reversal of the current first observed."

"I am aware that the mere contact of a metallic wire in a salt solution (electrolyte), even if unheated, at times suffices to set up a momentary movement of dissociated ions in the electrolyte, that is to say an electric current. But such was not the case in my first series of experiments as no current was indicated on the milammeter." The experiment shows that either heat or rotation may set up an electrical current within the canal, and that this may stimulate the crista ampullaris.

HUNTER, Philadelphia.

A Case of Lethargic Encephalitis. C. I. Urechia and N. Elekes, Arch. gen. di Neurol. Psichiat. e Psicoan. **4-5**, 3-4, 125 (Sept.) 1924.

The authors report a case of epidemic encephalitis with necropsy, in which marked hypothermy besides the rare symptom of othematoma was observed during the course of pneumonia, from which infection the patient died.

A woman, aged 29, at first showed mental confusion followed by a maniac and then a dementia praecox phase; during the last stage of the disease she had an othematoma and general rigidity without tremor. The spinal fluid, which was examined at three different periods, was negative. During the last month of life the patient showed marked hypothermy, and died from pneumonia without fever.

At necropsy the authors found intense alterations in the nuclei of the tuber cinereum, a condition which suggested to them the existence of a correlation between the lesions of the vegetative carrefour and the paralysis of the thermic centers.

The extrapyramidal pathways were the seat of intense alterations, the globus pallidus being far more profoundly altered than the substantia nigra. This finding suggested to the authors the possibility that the absence of tremor was due to the less intense alterations of the substantia nigra. In fact, the hypothesis has already been voiced that the rigidity is connected, principally, with a lesion of the globus pallidus, and the tremor with lesions of Soemmering's substance.

In the striatum the alterations were also marked, but the inflammatory process was far more pronounced than in the globus pallidus in which the degenerative process was especially dominant. In spite of so much alteration of the striatum, the patient did not present tremor. In the presence of a concurrent lesions of the two systems, the neostriatum and the archistriatum, the authors believe that the rigidity predominates.

Another interesting point in this case was the inversion of the neuroglia reaction in the cortex. Contrary to the rules of neuroglia pathology, while the neuroglia of the white matter showed a relatively moderate hypertrophy, that of the gray matter showed enormous proliferation with cells of two or three nuclei, frequent fibrils of elongated and abnormal forms suggesting the gliocyte found in lobar sclerosis and diffuse sclerosis. The gliosis is far more intense than that found in general paralysis or in other inflammatory diseases.

Naccarati, New York.

The Technic of Operations for Abscess of the Brain. Charles A. Elsberg, Arch. Otolaryngol. **1**:14 (Jan.) 1925.

The author advises against approach of the abscess through the wound of a previous operation as in mastoid disease, and recommends a separate opening in an aseptic field. The presence of a lining wall is a great factor of safety in both acute and chronic abscess. Acute cerebellar abscess rarely has a limiting membrane, but acute temporal lobe abscess and chronic temporal and cerebellar abscess usually have a membrane. "In the abscess which occurs as a complication of frontal or ethmoidal sinus disease, a distinct abscess wall is often present, while in the acute intracranial suppuration that follows infection within the orbit, the abscess, generally in the homolateral frontal lobe, is usually without any lining membrane."

Abscess secondary to osteomyelitis of the cranial bones, injury of the skull or brain, is usually superficial and has a distinct lining wall. Brain abscess secondary to pulmonary suppuration or bacteremia is usually multiple and without a limiting wall.

Slight flexor spasm at the knees with rigidity of the neck and an increase in the cells in the spinal fluid, if mainly lymphocytes, are not a contraindication to operation. Patients with pus and bacteria in the fluid "seldom if ever recover" and should not be operated on.

Local anesthesia should always be used, except in children or delirious patients. An osteoplastic flap should not be made, but the opening should be made as small as possible to prevent hernia of the brain, and a liberal opening should be made in the dura. Aspiration of the brain should be practiced with a needle with a rounded end only, in order to detect the lining wall if there is any. The surrounding area is packed with iodin gauze to prevent meningitis and a large rubber drainage tube is inserted and well fastened to the scalp with silk sutures. It should not be removed until all drainage of pus has ceased, usually after several weeks. It should be gradually shortened before being removed entirely.

In abscess without a limiting membrane the opening in the skull is made larger (5 by 6 cm.), the dura is opened widely and a piece of rubber dam is inserted, it is well packed with gauze, the cavity being kept wide open.

This important change in technic in abscess without a lining membrane has resulted in saving patients who formerly would have been considered hopeless.

HUNTER, Philadelphia.

RELATION OF ABSENCE OF SENTIMENTS AS OUTLINED BY SHAND TO SOME CASES LABELED PSYCHOPATHIC PERSONALITY. SAMUEL N. CLARK, Am. J. Psychiat. **4**:135 (July) 1924.

The author reports the case of a patient whose maternal uncle was a hard drinker and whose maternal aunt and cousin were insane. Early development was apparently negative; the patient was sociable, not easily excited, but early evidenced untrustworthiness. He left school at the age of 15 when in the seventh grade. He was a "bad boy" in school, smoking, playing truant and beginning to drink. He worked as a watchmaker for two years, was difficult to control, and after the death of his father never worked regularly again, learned to repair motors but did not stick to the job, told absurd lies, drank to excess at 19, and at 25 was sent to the house of correction for being drunk and carrying concealed weapons. Soon after this he was sent to the penitentiary for robbery, was released in 1917, and married in 1919, but never supported his wife. He stole from his mother. He was finally committed to a state hospital, where physical and mental examinations were negative. He soon became a trusty patient and did much work about the hospital. He explained that he never did anything bad except when intoxicated; that he did not care about drinking, but was led into it by friends.

The author characterizes the life of this psychopathic person as one without aim. The difficulty was apparently based on an absence of "sentiments," as conceived by Shand and developed by McDougal. The instincts are inherent, but sentiments are developed and centered about particular, concrete objects or abstractions, giving to them a fixed value as determining influences in the behavior of the individual. While the instincts are a common heritage, sentiment in this sense is a personal development and motivates behavior. Care must be

taken not to confuse this conception of the sentiments with the common usage of the term; they are much more comprehensive and stable. Psychopathic traits in the case described arose out of the patient's failure to develop sentiments. The ability to determine conduct cannot be measured by the bare statements of the individual, but must be reflected in what he really desires and actually does. The formation of these controlling sentiments on the part of the individual are the stabilizing influences which make social life possible.

READ, Chicago.

THE PARAFFIN REACTION OF THE CEREBROSPINAL FLUID. V. KAFKA, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:652, 1925.

Kafka has chosen a paraffin solution for investigation of the cerebrospinal fluid on account of the purity, cheapness and simplicity of its chemical structure. He dissolves 0.3 gm. paraffin with a melting point of 50 to 52 degrees (the American product) in 100 c.c. of absolute alcohol with the aid of heat. On cooling, some of the paraffin is deposited. This is the mother solution. When the test is to be made the necessary amount of this solution is mixed quickly with the same amount of distilled water at a temperature exactly that of the melting point of the paraffin. A turbid solution results that will not decompose. It may be used immediately. The spinal fluid to be tested is diluted progressively with 0.3 per cent. sodium chlorid solution; 0.75 c.c. of this solution is placed in the first tube, and 0.5 c.c. in each of the other nine tubes of the series. To the first tube is added 0.25 c.c. of the spinal fluid; 0.5 c.c. is then pipetted from the first tube into the second tube, mixed, and then 0.5 c.c. carried from the second to the third tube, and so on down the line as in any other colloidal test. Finally, to each of the tubes is added 1 c.c. of the paraffin solution preparation. A double quantity of fluid in the first tube is sometimes advisable in examining treated cases. Room temperature is the optimum. Time relationships are not mentioned.

A positive reaction is a clearing of the emulsion with deposit of the paraffin at the top. The reaction lends itself well to reading. Kafka distinguishes six degrees of precipitation. The curves resemble those found by other methods. Typical general paralysis is 6666652100; meningitis 0123532100; cerebral syphilis and tabes 0243100000.

Kafka gives the following advantages of his method: the small amount of fluid necessary, the simplicity of the technic, the needlessness of any preliminary test with salt, cheapness and relatively good legibility. "Whereas the gold sol. and the mastic reactions tend to show greater peculiarities in their curves, for smaller laboratories, and for the purpose of comparison, the paraffin reaction is to be recommended. It is especially good for the recognition of normal fluids."

FREEMAN, Washington.

SPLANCHNIC ANESTHESIA: AN ANALYSIS OF FORTY-TWO CASES. WILLIAM R. MEEKER, Arch. Surg. **10**:699 (March) 1925.

From the experience of those using local anesthesia, it seems that the pain experienced by the patient undergoing an abdominal operation under this type of anesthesia is caused by stimulation of spinal and not sympathetic nerve filaments, since it arises as the result of either traction on the mesenteries or from direct irritation of the parietal peritoneum. Paravertebral block of the fifth dorsal to third lumbar nerves for intra-abdominal anesthesia is anatom-

ically and physiologically correct but entirely unpractical. To subject a patient just prior to a severe abdominal procedure to a technic which involved the performance of at least twelve and possibly of twenty-two lumbar punctures hardly leaves him in a proper state of mind for further surgery.

Apparently the abdominal viscera are insensitive to pain so far as the cutting, crushing or cauterizing of an operation is an inadequate stimulus for the production of such pain. The breaking of conductivity in the splanchnic nerves for the relief of visceral pain in abdominal operations is therefore not in accordance with sound principles of anatomy and physiology. Furthermore, clinical experience with splanchnic anesthesia proves it to be inefficient, since by its use a complete surgical anesthesia of the abdominal cavity is not produced. The anesthesia must frequently be fortified by the administration of general anesthetics. Splanchnic nerve block is the least important of all the factors concerned in the success of an abdominal operation under local anesthesia.

To the fact that the intra-abdominal anesthesia produced by this method is inadequate must be added the dangers accompanying the method. There have been four deaths in 1,375 cases, due in all probability to the toxic effects of the large amount of solution necessary to block the nerves.

GRANT, Philadelphia.

INTRODUCTION TO A SYMPOSIUM ON FREUD'S METAPSYCHOLOGY. ERNEST JONES, Internat. J. Psycho-anal. **6**:1 (Jan.) 1925.

Jones' remarks are contributed as an introduction to a symposium on metapsychologic aspects of psychanalytic technic and theory, held at Salzsburg, Austria, at the Eighth International Psychoanalytic Congress, April 21, 1924. The term metapsychology as used by Freud includes the three aspects which must be considered in regard to any mental operation in the light of analytic psychology, namely, (1) the topographic, the region of the mind in which the operation takes place, whether in the unconscious, foreconscious or conscious; (2) the dynamic, that is, the value and the purpose of the thought; (3) the economic, the amount of energy with which the operation is invested. The papers of the symposium by Drs. Hans Sachs of Vienna and Franz Alexander and Sandor Rado of Berlin are of such a highly technical character that they do not lend themselves well to abstracting.

Dr. Jones, however, points out that one of the most important contributions of psychanalysis has been that it interpolated the infantile in the series of factors regarded as etiologically significant in the production of mental disease in addition to the preinfantile and postinfantile. In the pre-Freudian era the inherited and congenital factors, or the postinfantile occurrences, had been accorded most attention. Freud, however, was not unbalanced by the importance of his discoveries of the infantile phenomena, as a lesser man than he might have been. Necessarily he has written more extensively about the infantile factors which are concerned in his own discoveries, but he has not underestimated the force of current influences and ever has been alert to etiologic inferences which might seem warranted from phylogenetic history. In psychanalytic technic and theory Jones pleads for a combination of "scientific open mindedness and cool skepticism" toward conclusions, "which would shift the emphasis in etiology" away from the infantile.

OBERNDORF, New York.

THE DIFFERENTIATION OF ISOLATED CHICK PRIMORDIA IN CHORIO-ALLANTOIC GRAFTS. III. ON THE SPECIFICITY OF NERVE PROCESSES ARISING FROM THE MESENCEPHALON IN GRAFTS. LEIGH HOADLEY, J. Exper. Zool. **42**:163 (May 5) 1925.

The mesencephalon of a 48 hour embryo was removed and placed either around or next to the last somites of the same embryo on the chorio-allantoic membrane of an 8½ to 10 day chick. The somitic region was from one side only and was free from the primordial nerve cord, so that any innervation of the parts would of necessity come from mesencephalic tissue. After about a week's growth on the chorio-allantoic membrane, the host egg was opened and the graft examined histologically. It was found that nerves originating in the mesencephalon extended to and entered masses of tissue composed of mesonephros, cartilage, and connective tissue and voluntary muscle, often traversing long stretches of the host mesenchyme in the course of their growth. The variety of tissues which they entered showed that there was no great specificity in the effect of any tissue on them or of the functional developmental potentiality of the nerve cell. It was also found that where the nerve processes left the mesencephalon with only mesenchyme near them, they ended blindly a short distance from the point at which they left the mesencephalon. When some developing and differentiating tissue of the somitic region was present, these nerve bundles attained a much greater length. The morphologic differentiation of the nerve cells was not altered in cases in which nerves were formed. A dynamic conception of the factors causing the development of nerves and their growth toward their end organs as opposed to a purely chemical explanation is indicated by the results of the experiments. The dynamic conception of the development of the nerve cell is favored also by the differentiation of the ganglion of the neural crest isolated in the mesenchyme of the host membrane.

WYMAN, Boston.

RESULTS OBTAINED BY THE INTENSIVE USE OF BROMIDES IN FUNCTIONAL PSYCHOSES. WILLIAM W. WRIGHT, State Hosp. Quart. **10**:200 (Feb.) 1925.

Encouraged by the work of Ulrich and Klasi, the author treated depressed and agitated patients with large doses of sodium bromid. The drug was given until the patient approached a state of delirium and was then, as a rule, gradually withdrawn. The degree of tolerance was established for each patient, the dose ranging from 50 to 300 grains (3.25 to 19.5 gm.) a day; toxic symptoms were combated with saline solution by mouth. A number of cases are cited, most of them chronic and of the "disturbed ward" type. It was found that patients showing habit deterioration, with soiling, wetting, destructiveness, etc., were better able to care for themselves and less given to violent outbreaks. The agitated, depressed types showed less agitation, took food more willingly, and some recovered. In some showing a marked regression the attack terminated. Bromid rashes were rare. In many instances the drug seemed to act as a tonic, and the patients gained weight. The author feels that the therapeutic effect is the lessening of a state of tension which existed in all his patients given this treatment. He further reasons that one of the fields in which the free flow of energy is inhibited and causes a state of tension is the sexual field, and, since one of the physiologic effects of bromid is to depress or inhibit the sexual function, its administration in these states will release this tension and permit a return to normal. If bromid will release one tension, may it not also be expected to release other tensions?

HOWARD, Milwaukee.

MENTAL HEALTH PROBLEMS IN SCHOOL CHILDREN. FRANKLIN G. EBAUGH, Am. J. Dis. Child. **28**:265 (Sept.) 1924.

The author studied a series of fifty children of the school age presenting various kinds of mental problems, chiefly types of delinquency and emotional difficulties. In each case a complete physical examination was made, and the mental status and environment studied. With knowledge obtained from such a survey, the lines of therapeutic advice for each child were readily worked out: measures to effect physical improvement by treatment of the associated medical and surgical problems; reeducation of parents to secure the proper home training; and finally dealing with the child himself in order to remold the personality and solve his conflicts. The author finds considerable reason for encouragement when surveying the therapeutic results obtained after one year's treatment, and finds in the plasticity of the child, his suggestibility and ready response to encouragement and rational discipline every reason for obtaining gratifying results. The problem, complicated as it is by the factor of environment, requires the consideration of the child as an individual and the cooperation of the physician, visiting nurse and social worker for its satisfactory solution. School clinics operating in close cooperation with mental clinics of the district and children's observation wards in general hospitals are recommended. The importance of the treatment of the maladjusted child is particularly stressed as a prophylactic measure against the development of abnormal reactions and psychoses in the adult.

VONDERAHE, Cincinnati.

CONCERNING THE SUDDEN ONSET OF SYMPTOMS IN BRAIN TUMORS. GEORGE WILSON and N. W. WINKLEMAN, Atlantic M. J. **28**:285 (Feb.) 1925.

The authors present a clinical and pathologic study of seven cases of brain tumor, all of them gliomatous in nature, in which sudden symptoms appeared either spontaneously or following trauma or acute alcoholism. It is pointed out that the attacks strongly simulate apoplexy, but in patients under 40 years of age without cardiovascular involvement, apoplexy is rare; this should be considered of diagnostic importance. Three of the patients whose cases were reported were under 40. Acute alcoholism was present in one case, trauma in one case, rapid development of stupor without a known cause in four cases. The tumors were variously placed and of considerable extent, and all showed hemorrhage either into the tumor or into the surrounding area. The authors call attention to the danger of lumbar puncture in this type of case and advise, if the pressure is found to be high without evidence of meningitis, that no fluid be withdrawn. The appearance of symptoms is frequently without previous indication of an intracranial lesion, and appropriate tests should be made in all doubtful cases of vascular lesions of the brain to rule out the possibility of a hemorrhage into a tumor. Surgical intervention offers palliative relief, and when acute symptoms from hemorrhage into a tumor appear it is usually the index of a terminal condition.

FAY, Philadelphia.

EXOPHTHALMOS AS A COMPLICATION OF NASAL SINUSITIS. C. F. YERGER, Arch. Otolaryngol. **1**:415 (April) 1925.

Exophthalmos is a rare complication of sinusitis. Usually the frontal in adults is involved and the ethmoid in children. It may be due to an increase in the contents of the orbit as in cellulitis or pus or to diminution in size of the orbit due to pressure of a mucocele or pyocele. Of the seven cases

quoted, only one showed pus in the nose. Four patients recovered and three died. The mode of invasion is by direct continuity or by thrombophlebitis or infection through the small veins common to both the sinuses and the orbit. "The most frequent cause of unilateral exophthalmus is sinusitis." We have two types, one with acute onset and the signs of an abscess, the other with gradual onset and the signs of pressure behind the ball. The nose may appear normal in many of these cases because of a closed empyema of one of the sinuses, the drainage of the sinus by a previous discharge of pus through the nose leaving a healthy appearance, or the pus may have been evacuated from the sinus to the orbit or to a subperiosteal abscess. Other causes of unilateral exophthalmos are trauma, infection about the head, orbital neoplasm, syphilis, hemorrhage, cavernous sinus thrombosis, extensive tenotomy and goiter. The treatment is immediate operation before intracranial complications set in. The operation of choice is the external one with attention to the involved sinuses and any intranasal sinus that is indicated.

HUNTER, Philadelphia.

SOME OBSERVATIONS ON THE TYPES OF BLOOD-SUGAR CURVE FOUND IN DIFFERENT FORMS OF INSANITY. K. K. DRURY, J. Ment. Sc. **71**:8 (Jan.) 1925.

The authors have examined the sugar tolerance of 100 patients in a county hospital for mental diseases. The results are given according to diagnoses, and this has an unfortunate side, as it leaves the condition of the patient undetermined inside certain groups. It would have been better if the patient's symptoms on the day of examination had been described. Perhaps the "confusional" group of the authors is the best limited, as manic-depressive and dementia praecox states have been ruled out. Five patients in this group show a normal fasting level but no return to the starting level in two hours. Patients with melancholia at the climacteric have a high fasting level of the blood sugar. In acute cases of dementia praecox, broad curves like those in confusion psychoses were found, and in chronic cases the curves were small and low. The general conclusion is reached that the blood sugar curves show more variation in patients with mental disease than in normal people.

BOND, Philadelphia.

FURTHER OBSERVATIONS ON THE ANGULAR TRANSPLANTATION OF THE NEURAL TUBE OF AMBLYSTOMA. H. L. WIEMAN, J. Exper. Zool. **41**:471 (April 5) 1925.

When a section of the neural tube of amblystoma, together with parts of adjacent somites, is excised and reimplanted in a position at right angles, restoration of anatomic connections between neural transplants and stumps occurs in a shorter time when the operation is performed in the region of somites II to IV than at more posterior levels. When the transplant is embedded at an angle of 135 degrees in the region of somites III and IV, the result is similar to that obtained from transplantation at 90 degrees in more posterior levels, owing, presumably, to a greater antagonistic action of a secondary metabolic gradient, in the transplant, to the principal metabolic gradient of the embryo. The results afford evidence in support of the view that nervous union between transplanted neural tube and stumps depends primarily on the development of descending outgrowths from the anterior stump. The setting up of a metabolic gradient at an angle of 135 degrees to the principal gradient inhibits the formation of descending connections to a greater extent than when the gradient of the transplant forms an angle of 90 degrees.

WYMAN, Boston.

FETICHISM AND CONDITIONED REFLEXES. M. LAIGNEL-LAVASTINE, Folia neuropath. Esthoniana **3**:158, 1924.

Freudian theories of the transfer of the affect following psychic trauma give a general explanation of fetichism.

At the sight of meat, the dog secretes gastric juice. The sight of meat is associated with a red light. At each repetition of the double stimulus, the same reaction takes place. In the third part of the experiment, the meat is left out, but the red light is preserved. The sight of this brings about the same secretion as before. This reflex, at first conditioned by the specific stimulus, is now elicited in the absence of the specific excitant by some other stimulus which has arbitrarily been associated with the specific stimulus during a certain number of tests.

The analysis of the picturesque conditions attending the first sexual adventures explains the curious behavior of the fetichists. Some object has caught the attention at the moment of sexual pleasure, and afterward its memory is linked with the emotional memory. It is one of the examples of the great laws of sensory-emotional association which is at the bottom of all poetry.

Fetichism seems to be a specialized expression in the sexual sphere of conditioned reflexes. Similar conditioned reflexes may play a part in other sexual perversions.

FREEMAN, Washington.

SCOPOLAMIN SLEEP IN PSYCHIATRIC WORK. P. R. VISSIE, State Hosp. Quart. **10**:238 (Feb.) 1925.

It is the author's opinion that scopolamin will produce a cerebral depression, and at one time during this depression there is present an apparent border state between sleep and wakefulness. At this time there is an interruption of the current of associative reasoning that inhibits the imagination, causing a suspension of the patient's will, and he is consequently unable to protect himself by deceit. Following the method of House, a number of psychiatric patients were subjected to scopolamin sleep and then questioned. Several of these were suffering from dementia praecox of the catatonic type. They responded only slightly to the questioning, and after the sleep returned to their former condition. Slightly better results were obtained in depressed praecox cases and in a few highly excited patients. Certain delusions, trends of thought and sense falsifications were brought to light as well as other facts concerning the patient that could not be ascertained otherwise because of the mental condition. The procedure in some instances seemed to be a starting point for improvement.

The various methods that have been used to produce artificial amnesia are reviewed, and the author feels that the use of scopolamin is superior to any of the others.

HOWARD, Milwaukee.

THE DIFFERENTIATION OF ISOLATED CHICK PRIMORIDA IN CHORIO-ALLANTOIC GRAFTS. II. THE EFFECT OF THE PRESENCE OF THE SPINAL CORD, I. E., INNERVATION, ON THE DIFFERENTIATION OF THE SOMITIC REGION. LEIGH HOADLEY, J. Exper. Zool. **42**:143 (May 5) 1925.

The last five segments of chick embryos in front of the segmental plate were transplanted to the chorio-allantoic membrane of 8½ day to 10 day old chicks at the union of two of the larger blood vessels. The parts transplanted were of two types: one with the primordium of the nerve cord removed and one in which it was left intact. The donors of the transplanted tissue were

of 36 and 48 hours of incubation. The grafts were allowed to develop for about a week, when the egg of the host was opened and the grafts studied in toto and in sections. The primordia of both types of transplants developed their normal differentiation. The presence or absence of the primordium of the spinal cord seemed to have no effect on the differentiation of the cells as units of structure or of the differentiation of primordia as units. This applied to all of the primordia examined, even to the development of the spinal ganglions from the neural crest. The general orientation of closely associated parts was maintained as in the normal. This justifies the conclusion that neither sensory nor motor innervation is essential for the primary differentiation of the somitic region of the chick.

WYMAN, Boston.

REMISSIONS IN GENERAL PARALYSIS. M. W. RAYNOR, State Hosp. Quart. **10**: 67 (Nov.) 1924.

A series of 1,004 patients with untreated general paralysis, admitted between July, 1911, and June, 1918, were studied as control material for patients under treatment. Of the entire group, 78 per cent. died during residence at the hospital; eighty-four patients were discharged as improved. By improvement the author refers to a change in the clinical picture, but with continuation of symptoms that rendered the patient unable to engage steadily in remunerative occupation. By the term remission is meant return of physical vigor, no ataxia in ordinary movements, disappearance of conduct disorders and a more or less stabilized emotional state. Thirty-three patients had remissions. The average duration of the remissions was about three years. Remissions may occur more than once in the course of the disease and are more common in patients presenting a gradual onset with changes in disposition and emotions, and defects in orientation and memory than in other clinical types. No anamnestic, mental, or neurologic criteria were found on which a prognosis for remission could be based.

HOWARD, Milwaukee.

HYPNOSIS WITH DIRECT PSYCHOANALYTIC STATEMENT AND SUGGESTION IN THE TREATMENT OF A PSYCHONEUROTIC OF LOW INTELLIGENCE. JOHN J. B. MORGAN, J. Abnorm. Psychol. **19**:160-164 (July-Sept.) 1924.

A girl, aged 17, with an intelligence quotient of 8, under hypnosis expressed a conflict betwen an infantile type of morality and the normal sex impulses of puberty. The proper solution of this conflict was impressed under hypnosis. A cure, so far as the conduct of the patient was concerned, was evident six months after the treatment. This recalls the foolish acerbity with which its opponents attacked psychanalysis, and the equally foolish need that analysts seemed to feel in denying the terrible accusation that, after all, the therapeutic value of the freudian procedure was only suggestion dressed up in another form. The consensus of opinion of the New York psychanalytic school, reflecting the pictures presented by Freud and Rank, seemed to be that much more active interpretative activity (or suggestion—my words) was called for on the part of the analyst.

HAMILL, Chicago.

OLFACTORY CONNECTIONS IN THE ALBINO RAT, WITH SPECIAL REFERENCE TO THE STRIA MEDULLARIS AND THE ANTERIOR COMMISSURE. ELISHA S. GURDJIAN, Jour. Comp. Neurol. **38**:127 (Feb.) 1925.

This study is preliminary to a detailed study of the thalamus of the rat and supplements Cajal's exhaustive analysis of the brain of the mouse. It

is based chiefly on sections prepared by the pyridin-silver and toluidin blue methods. Perhaps the most significant general conclusion is the emphasis on the complex character of the anterior commissure. The lateral olfactory areas of the bulb and the hemisphere on the two sides are interrelated throughout their entire extent by commissural and probably by decussating fibers as well, from the olfactory bulbs to the posterior poles of the hemispheres. The analysis of the stria medullaris and stria terminalis is good though doubtless by no means complete, for these fiber systems are exceedingly complex.

C. J. Herrick, Chicago.

An Unusual Sequel of Meningitis. Lesion of the Conus Medullaris. Lawson Wilkins, Am. J. Dis. Child. **29**:67 (Jan.) 1925.

The author reports a case of epidemic cerebrospinal meningitis in a child aged 2½ years, from which it apparently recovered. Two years later, however, the child was returned for treatment of an ulcer which had developed in the anal fold. Examination at this time revealed an area of total anesthesia of the peri-anal region; the external sphincter appeared to be relaxed, and the anal and the gluteal reflexes could not be obtained. The remainder of the general and neurologic examinations were negative. A diagnosis of a lesion of the conus medullaris, resulting from meningitis was made. The author notes that in very young children the spinal cord may extend to the level of the fourth lumbar vertebra, and therefore that the lesion may have resulted from trauma due to lumbar puncture rather than from meningitis.

Vonderahe, Cincinnati.

Tabes Diabetica. Ralph H. Major, J. A. M. A. **83**:2004 (Dec. 20) 1924.

The case reported is evidently a typical example of the complication of diabetes mellitus often referred to as pseudotabes or tabes diabetica. The patient had been ill for six years; two years ago, he began to be ataxic, and at the time of examination he showed an extreme ataxia, a tabetic gait and marked sensory disturbances, together with sharp shooting pains in the legs.

The pupillary reactions were not typical of tabes dorsalis, although there was a sluggish response to light. The knee reflexes were exaggerated. A striking feature was marked improvement with dietary restriction and insulin therapy. The author states that it is difficult to believe that the patient could have had so much degeneration of the posterior columns as described by Williamson and Sandmeyer and have recovered so promptly from his tabes-like symptoms.

Nixon, San Francisco.

On the Growth of the Human Eyeball and Optic Nerve. R. E. Scammon and E. L. Armstrong, J. Comp. Neurol. **38**:165 (Feb.) 1925.

The original observations include measurements of the eyeballs of seventy-one fetuses. Data on postnatal growth were collated from the literature and the whole mass of data subjected to statistical analysis. The growth in volume of the eyeball in the fetal period follows the general course characteristic of the volume of the body as a whole. More specifically, the growth is almost similar to that of the spinal cord and brain stem. The eyeball a little more than doubles its weight between birth and maturity. Most of this growth is made in the first five years of postnatal life. No definite evidence was found of a pubertal increase in the weight of the eyeball. It is estimated that the

coats of the eye form the greatest part of the postnatal growth, the contents of the bulbus, including the lens, comes next, and the cornea makes the least postnatal increase.

C. J. Herrick, Chicago.

The Effect of Iodin in Exophthalmic Goiter. P. Starr, H. P. Walcott, H. N. Segall and James H. Means, Arch. Int. Med. **34**:355 (Sept.) 1924.

Forty-two cases of exophthalmic goiter comprise the series on which this study is based. The patients were kept in bed, and the compound solution of iodin (liquor iodi compositus, U. S. P.) was administered after meals, the usual dosage being 15 drops daily. An abrupt remission of the disease characterized by a lowering of the basal metabolic and pulse rate, increase in weight and diminution of symptoms occurred in more than 80 per cent. of the patients. The iodin apparently does not suppress the disease permanently, and when its use is discontinued toxic symptoms recur within from one to two weeks.

Vonderahe, Cincinnati.

The Weight of the Brain, of Its Parts, and of the Spinal Cord of the Frog, Turtle, and Dog. Homer B. Latimer, J. Comp. Neurol. **38**:49 (Dec.) 1924.

The weights of the parts of the brain in percentages of the weight of the entire brain are given in the following table:

	Frog	Turtle	Dog
Prosencephalon	50	67	83
Mesencephalon	24	12	2
Medulla and pons	—	16	5
Cerebellum	—	5	10
Rhombencephalon	26	21	14
The percentages of brain to body weight are	0.2	0.09	0.8
The percentages of spinal cord to body weight are	0.1	0.1	0.1

C. J. Herrick, Chicago.

Brain Abscess: Report of an Unusual Case. M. G. Peterman, Am. J. Dis. Child. **28**:208 (Aug.) 1924.

The case reported here is one of a staphylococcic abscess of the left frontal lobe in a child of 11 years. The onset was characterized by frontal headache, vomiting and a slow pulse. The misleading features of the case were: a history of phlyctenular keratitis seven years previously, a positive Pirquet reaction, lymphocytosis in repeated spinal fluid examinations, positive Kernig and Brudzinski signs and absence of any antecedent acute infection. While the clinical evidence apparently pointed to a tuberculous involvement of the meninges, necropsy revealed a frontal lobe abscess which yielded a staphylococcus in pure culture.

Vonderahe, Cincinnati.

The Study of the Undivided Personality. Gordon W. Allport, J. Abnorm. Psychol. **19**:132-141 (July-Sept.) 1924.

Personality is more than a summation of its analyzable parts. The relation of the parts to each other establishes the identity. The more intimately we know a person, the more frequently are we conscious of his general personality or form quality. But this knowledge is not of a kind that can be checked

or experimentally proved. We apprehend personality, not by analysis, but by empathy — an understanding of the general driving forces behind the individual.

HAMILL, Chicago.

A CASE OF SCAPHOCEPHALY WITH MALFORMATIONS OF THE SKELETON, AND OTHER TISSUES. MARIAN C. PUTNAM and K. F. PELKAN, Am. J. Dis. Child. **29**:51 (Jan.) 1925.

The case reported here presents an unusual association of skeletal anomalies with other abnormalities of development. The child was first seen when it was about 1 year old. Delivery was normal. There were three other healthy children in the family. The family history was negative. The head of the child was scaphocephalic in type, about normal in width and height, but conspicuously long owing to the prominent forehead. The child in addition presented a marked dorsolumbar kyphosis, short heavy bones, limitation of movement of the elbow and shoulder, pot belly, redundancy of superficial tissues, hypertrichosis and corneal clouding.

VONDERAHE, Cincinnati.

INSTINCT, HABIT AND INTELLIGENCE IN SOCIAL LIFE. SEBA ELDRIDGE, J. Abnorm. Psychol. **19**:142-154 (July-Sept.) 1924.

The article is a review of the attitude taken by three schools of writers toward the question as to where the emphasis should be placed. One gains the impression that the argumentation of the scholastics has its progeny even as the scientific spirit of Galileo has. The author advises a middle-of-the-road attitude, recognizing the importance of the force of both instinct and habit in driving and of intelligence and education in shaping the conduct of man.

HAMILL, Chicago.

HYPOGLYCEMIA AND ACIDOSIS IN FASTING CHILDREN WITH IDIOPATHIC EPILEPSY. EDWARD B. SHAW and MARGARET MORIARTY, Am. J. Dis. Child. **28**:553 (Nov.) 1924.

The authors studied five cases of idiopathic epilepsy in children who were subjected to a complete fast lasting from ten to fourteen days. During this time nothing was given to them except water, administered on a basis of 75 c.c. per kilogram of body weight every twenty-four hours. The results of their studies show in all instances an increase in blood uric acid, a moderately marked acidosis and a striking decrease in blood sugar. During the latter days of the fast a slight diminution in the degree of acidosis and a tendency toward a rise in the blood sugar was noticed.

VONDERAHE, Cincinnati.

THE OLFACTORY CENTERS IN CRUSTACEANS. BERTIL HANSTRÖM, J. Comp. Neurol. **38**:221 (April) 1925.

The central connections of the olfactory organs of the antennulae of several species of crustaceans are described in detail. Some of these species have well developed eyes and some degenerated eyes. The peripheral olfactory neurons are like those of vertebrates, and comparisons are drawn between the central olfactory connections of crustaceans and vertebrates.

C. J. HERRICK, Chicago.

PROGRESS IN EXPERIMENTS ON TACTUAL INTERPRETATION OF ORAL SPEECH. ROBERT H. GAULT, J. Abnorm. Psychol. **19**:155-159 (July-Sept.) 1924.

Under proper instruction, the vibrations of the waves of sound cause sufficient physical disturbance to be capable of recognition by the tactile organs of the skin of the palm of the hand to an extent that permits apprehension of spoken words. The experiments recorded were made with a normal hearing man.

HAMILL, Chicago.

THE POSTNATAL GROWTH OF THE CENTRAL NERVOUS SYSTEM OF THE CHICKEN. HOMER B. LATIMER, J. Comp. Neurol. **38**:251 (April) 1925.

This is a detailed statistical study of the growth of the brain and its parts and of the spinal cord.

C. J. HERRICK, Chicago.

HALLUCINATIONS IN CHILDREN. MANDEL SHERMAN and BERT I. BEVERLY, J. Abnorm. Psychol. **19**:165-170 (July-Sept.) 1924.

This article records the appearance of hallucinations in children and accepts their relationship to lack of the intellectual control of imagination.

HAMILL, Chicago

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Monthly Meeting, Feb. 19, 1925

WILLIAM HEALY, M.D., *President, in the Chair*

THE EXPERIMENTAL PRODUCTION OF RIGIDITY WITH BULBO-CAPNINE. DR. HUGO MELLA.

DeJong has shown that the tremor of paralysis agitans can be controlled by the use of bulbo-capnine and that in larger doses a hypertonic catatonic-like syndrome may be produced in cats. (Demonstration of cat under the influence of bulbo-capnine.)

DISCUSSION

DR. K. M. BOWMAN: Does the cat become fatigued? Is there an element of fatigue?

DR. MELLA: I have kept one in that position from four o'clock one afternoon until the next morning. This cat will probably be in good condition late tomorrow morning. Some show signs of fatigue.

DR. BOWMAN: He apparently moves his head pretty freely.

DR. MELLA: Yes, but only within a small radius. If I had given him a little larger dose, I could have bent him like a piece of lead pipe, and his head would remain in any position that I might place it in.

DR. DONALD GREGG: What is supposed to be the site of the action of the drug, the central nervous system?

DR. MELLA: Yes, it must be. In a small dose it will stop tremor; in a little larger dose it will produce rigidity; in a still larger dose it will produce tremor, convulsions and death.

DR. E. W. TAYLOR: Why is it so difficult to raise the plant from which this drug is derived?

DR. MELLA: There is no difficulty in raising the plant. The difficulty lies in isolating this one alkaloid. There are eleven alkaloids in the plant, and bulbo-capnine is one of them. The bulbo-capnine of the U. S. dispensatory is not the pure alkaloid.

MENINGOCOCCUS MENINGITIS. DR. HENRY R. VIETS.

In spite of our knowledge that meningococcus meningitis is a disease of known etiology, and in spite of the fact that we have a specific form of treatment, both the diagnosis and the treatment are often uncertain, and the disease has a mortality of from 25 to 35 per cent. Definite information is needed concerning: (1) the entering pathway of the organisms; (2) the primary site of the lesion, whether it be in the blood stream, meninges, or ventricles; (3) the earliest clinical manifestations, especially the intermittent type of fever; (4) the proper locus for serum treatment, whether intravenous, intraspinal, intracisternal or intraventricular; (5) the cause of certain post-meningitic symptoms.

The following case illustrates many of the points in question:

A woman, aged 29, after a slight illness consisting of headache, slight purpuric rash on the extremities, joint pains and fever, was comparatively well for four weeks, except for three distinct periods when she had severe attacks of headache associated with rise in temperature to 101 or 102. These attacks lasted twenty-four hours, and each was preceded and followed by periods of practically no discomfort. The patient later developed signs of meningeal irritation, but a spinal fluid examination failed to show meningococci. A cerebellar exploration was made in the hope of discovering an abscess. No abscess was found, but the fourth ventricle, dilated, contained cloudy fluid from which no definite organisms could be grown. Two days later when the symptoms increased, combined ventricular and lumbar puncture was performed. Meningococci were found in both fluids, and serum was given into both the ventricles and the lumbar spine. Intraspinal serum was again given twenty-four hours later. The patient made an excellent recovery. When seen four months later, she showed no symptoms of the disease.

The slight illness with purpura, joint pains, headache and mild fever was probably the time of beginning meningococcemia. The three attacks of severe headache associated with increase of temperature are said to be characteristic of meningococcus septicemia. Meningococcemia cases have been described with this intermittent type of temperature lasting for many months before signs of true meningitis develops. It is considered possible in this case, however, that involvement of the central nervous system may have taken place through the choroid plexus and caused a ventriculitis early in the period of meningococcemia. In such an event, the severe attacks of headache and rise of temperature may have been caused by a temporary obstructive hydrocephalus. A diagnosis of meningococcus meningitis was not definitely established until meningococci were found in the lateral ventricles. It is possible that meningococcus meningitis always begins primarily as a meningococcemia and secondarily as a ventriculitis. If this is the case, as the foregoing history would indicate, early serum treatment into the lateral ventricles is indicated.

DISCUSSION

DR. E. W. TAYLOR: I am sorry that I do not recall the details of this case. I remember very well having seen the patient and that Dr. Viets and I were completely puzzled at the time concerning the diagnosis. The patient was obviously very sick, and I felt rather definitely that the prognosis was bad.

DR. J. B. AYER: I agree with Dr. Viets that it is likely the infection here was meningococcus septicemia, but this is not proved. Nor does it appear that he has proved that ventriculitis preceded the meningitis, although it seems that this may well have been the case. Leukowicz' work is strongly suggestive that ventriculitis precedes meningitis, but in some cases he obtained bacteria-free ventricular fluids when bacteria were present in the subarachnoid space. His conception that meningitis is merely a sequela of ventriculitis is radical, but perhaps correct. If he is right, our treatment of meningitis is wrong. Only by synchronous puncture of the ventricles and the subarachnoid space in early infections will this vital point be decided. Dr. Viets is to be commended for his persistence in attacking this particular infection.

DR. VIETS: Dr. Ayer's remarks followed my line of thinking. The evidence for thinking that perhaps the ventricle was primarily affected, as far as the central nervous system was concerned, was based on the fact that the first lumbar puncture showed no organisms and gave no cultural growth. Then

between that time and the ventricular puncture a cerebellar operation disclosed a block between the fourth ventricle and the subarachnoid space. The next day when another lumbar puncture was made organisms were found in the ventricle and also in the lumbar sac. If we had not opened up the pathway by the operation, I cannot definitely say that we would not have found organisms in the lumbar sac as we did later, but it seems likely that when we did open up the pathway the organisms passed from the ventricle into the spinal fluid.

We did not make an early diagnosis. Possibly we performed an unnecessary operation, but we maintained adequate drainage, which, perhaps, could not have been done except by operation, and we put our serum where it was needed most. Those are the two important points in the treatment of meningococcus meningitis.

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, March 13, 1925

ALBERT C. BUCKLEY, M.D., *President, in the Chair*

EXTENSION OF HOSPITAL ACTIVITIES TO THE EXTRAMURAL PATIENT. DR. H. W. MITCHELL.

The hospital for mental diseases situated in a district composed of several large but sparsely settled counties has an opportunity to render medical service that in most urban locations would be performed by other agencies.

The Warren State Hospital has for more than ten years opened its wards, at a nominal board rate, to all voluntary cases sent by physicians for the purpose of diagnosis and advice. All members of the county medical societies have been specially invited to send patients with early cases of suspected neurosyphilis either for diagnosis or for treatment. After the war neuropsychiatric examinations for the government were made for two years, the patients receiving clinical examination, laboratory study and maintenance for from two to five days in return for the usual examination fee.

The local physicians appreciate that the hospital staff is not engaged in practice and see patients only at their request, but that they can be called on for any charity work desired. This demand on the staff was met some years ago by establishing a weekly outpatient clinic at which any neuropsychiatric case would be received for examination and report.

Inmates for several homes for children have been studied with all available technic. Many hundreds of school children have been given psychometric tests and rating, and there is a growing demand for such service in nearby towns. The courts have sent many juvenile offenders to the hospital for study and report, as well as a lesser number of adults whose mental condition was in question.

Neuropsychiatric service has been given freely to various social agencies in their charitable work. A hospital physician serves as consultant on the dispensary staff of the Erie Associated Charities where the organization is such that careful medical work is possible through the aid of consulting specialists.

Social service work has been constantly employed since 1912, special efforts being made to secure adequate histories and to keep the paroled patient in touch with the hospital.

The medical routine, including sociologic, clinical and laboratory study, has been demonstrated to physicians in nearby counties by clinics and numerous papers on some phase of hospital work, so that the function of the hospital could be understood by the medical profession. In such manner the physicians of a country hospital may be able to render no inconsiderable service in communities in which there is no call for large clinics or opportunity for the academic teaching function. This type of hospital service also conveys to the general public in a practical way a better understanding of problems of mental hygiene than can be given by any other method.

The general public has requested many talks on mental hygiene serving to widen the usefulness of the hospital by increasing the demand for extramural service to the community.

COMMUNITY CLINICS AND INSTRUCTION UNDER STATE HOSPITAL SUPERVISION. DR. J. ALLEN JACKSON and DR. HORACE VICTOR PIKE.

A state hospital for mental disease should not limit its function to the treatment and care of the mentally ill patient committed from the community, but should extend its activities into its hospital district with a view of disseminating knowledge that will aid in the prevention, early recognition and treatment of the mentally diseased and mentally defective. This applies especially to institutions in rural communities where consultation and advice in matters relating to abnormal mental conditions are not so readily obtainable as in the large community centers.

For the carrying out of such a program there should be included in the hospital organization a department of community service which should be under the immediate direction of a director of clinical psychiatry, to whom should be assigned the extramural and intramural social service personnel and the clinical and educational work in the field at large.

In order to serve its community adequately, the extramural work should consist of two types of activities: first, clinical; second, educational. The clinical work may be best carried out by the organization of mental clinics at centers easily accessible to the general pubic and practically covering the hospital district. Such a mental clinic should represent a hospital unit in the field in the community which it serves. It should not be considered as an open door to a mental hospital or state institution for the feebleminded, but rather a consultation center for parents, physicians, social organizations, courts and schools for the recognition and recommendation as to treatment of the individual members of the community who are unable to adapt themselves to the social environment because of mental disorder or mental defect.

The educational work should include systematic instruction of various organized groups making up the community within the hospital district. Among these groups may be mentioned: parents and teachers, who may be reached through Parent-Teachers' Associations; prospective parents and teachers, through state normal schools, colleges and universities; physicians, through county and state medical societies; and clinical demonstrations in the wards of the hospital and the mental clinics in the field. The lay members of the community may be reached through addresses to Rotary, Kiwanis, Lions, college and civic clubs, and the discriminating distribution of a mental health bulletin to these groups as well as to overseers of the poor.

Such a program has been carried out over a period of practically four years at the Danville State Hospital. This institution serves twelve counties with a total population of 874,000, and at the present time eight mental clinics

are being conducted throughout this field. During the year 1924, 1,714 visits were recorded at these clinics, and of this number 875 were new patients. Two state normal schools, two universities and one college are having presented before their student bodies systematic courses of lectures on abnormal psychology and mental hygiene, at the close of which specially arranged clinics at the hospital are provided for the classes, and an inspection of the hospital is allowed. During the past year approximately 5,000 students have been so instructed. Courses of instruction on nursing in nervous and mental disorders are being presented before nurses in training in three general hospitals as well as in our own training school. Clinics for the 641 physicians in the hospital district have been conducted at stated intervals, and the general community, clubs and social organizations have had brought before them from time to time by the superintendent and clinical director material relative to mental hygiene.

Our experience at the Danville State Hospital in the organization and carrying out of such a program of community service activities has proved this work to be of inestimable value, not only to the community which the hospital serves, but also to the hospital itself and to the individual members of the medical staff who have assisted in its furtherance.

DISCUSSION

Dr. William C. Sandy: Before passing on the papers, I should like to recall to your minds what Dr. Mitchell said about the absurdity of the state being asked to support its institutions for the small sum of $5.31 a week per capita and yet keep up the high standards of hospital care and treatment. I also want to remind you that the legislature cut off $500,000 from the appropriation for the insane, which is a very serious thing, and every effort must be made to get this amount again. The total sum asked for represented the sum considered necessary after serious thought not only by the members of the budget committee, but also by the superintendents of the hospitals and the trustees, as well as being the result of years of survey. The only way we can get back this appropriation is by having our friends work from the outside. If this appeal can be brought to the representatives and senators, we will have some chance of getting this appropriation again.

In looking back on the progress we have made in Pennsylvania during the last few years, I am reminded of the story attributed to President Wilson; it concerns two men who were walking from New Haven to Bridgeport. After walking for an hour they asked a man how far it was to Bridgeport, and he said twelve miles. After walking another hour they asked a second man, and he said the distance was twelve miles; after still another hour they asked a third man how far it was to Bridgeport, and on being told it was twelve miles, one man said to the other: "Cheer up, its not getting away from us!" It seems to me, however, that sometimes it is getting away from us and that we are slipping back, and we can only depend on our friends to help us out in this serious situation.

The two papers just read represent some of the important work in mental hygiene being done by the state. I doubt that there is any more important work being done, and the interesting thing is that it shows that we are getting the patients when they are children—at a time which is most opportune for preventive measures. The educational activities have a far-reaching effect, as they plant the seeds of mental health in the minds of the embryo teachers. You have seen outlined the two methods of approach, both of which are being used

at most of our state hospitals; i. e., Dr. Mitchell's method of bringing the patients to the hospital and Dr. Jackson's idea of conducting the work as a community activity. We in Harrisburg find it a great convenience to have such facilities for referring patients in the northwestern part of the state, as Dr. Mitchell has outlined. I also wish to mention that, more and more, the judges are getting the habit of sending prisoners to the hospital for temporary observation.

I have been asked to discuss this subject more from the standpoint of what is going on in the state generally. From the beginning of the department in 1921, it has been the policy to stimulate the establishment of mental clinics. In 1921, there were seven such clinics; in 1925, there are thirty-eight regular and five occasional clinics. This has been made possible by the active cooperation and initiative of the psychiatrists in the institutions, on whom we have to depend to conduct the clinics.

The Bureau of Mental Health has three field representatives who are psychologists and social workers. They assist in the clinics and help to conduct preclinic work. We also have the cooperation of the educational department, especially their department representative, Dr. Maxfield, through whom all the superintendents of the schools are notified as to the clinic facilities. We also have the cooperation of the physicians through the secretaries of the county medical societies. More than 2,000 card reports of new cases seen at the clinics in 1924, were filed in the central office. These cards afford a continual survey or census of the feebleminded throughout the state as well as of the mental cases. The Bureau of Mental Diseases furnishes the cards and also the work sheets for the history taking. In the future, if the legislature grants the appropriation — which we sincerely hope it will — we expect to have facilities for a traveling clinic for the Northwest central district, which area at present is practically inaccessible so far as ordinary clinics are concerned. I also hope to have on my own staff another psychiatrist whose duties will be largely in the field. Incidentally, we have been cooperating with Dr. Pike — the acting medical director of the Public Charities Association — in the establishment of a course in mental hygiene in the various state normal schools, and in helping to interest the local psychiatrists in giving these lectures. These are about to be established at the California Normal School in the southwestern part of the state and also at Slippery Rock, Pa. We use the Danville Mental Hygiene Bulletin for publicity purposes from time to time, preparing articles, the reprints of which are distributed for propaganda. These are all evidences that the state hospitals are no longer asylums, which they are often called. You would be surprised at the number of times my scientific and professional sensitiveness is hurt by hearing the state institutions referred to as "asylums." It is discouraging and makes me want to get away from the whole business, because I know they are not asylums, and that the men are doing scientific work in them. The institutions are active forces for the prevention and treatment of mental diseases. Too little is known about their good work, and I hope that more frequently occasion will arise to inform the public as to what is taking place. It seems to me that Pennsylvania has an inferiority complex; when we go to National meetings we constantly hear what psychiatrists in New York and Massachusetts are doing. I believe they are doing nothing along these lines that is not being done here, and it is up to us to advertise the fact.

Dr. Buckley: The practical phases of the subject of applied psychiatry for the benefit of the community have been so adequately presented that I

can add only a few words in support and encouragement of the good work being done by the hospitals under the supervision of the state institutions. We have for some time known that state hospital directors have long since passed out of the field of farm managers and buyers of potatoes, and have passed into the field of scientific medicine and are contributing some of the very best work which is produced along these lines. The question of who should be educated along these lines first, the physician or the layman, seems to me to be similar to the question of which comes first, the hen or the egg. I think both sides afford material for discussion, and that there is equally good work being done from both standpoints.

Dr. Edward A. Strecker: While we knew in a general way of the remarkable progress that has been made in the state hospitals and their outside activities, I did not think we realized how much had been accomplished until we heard these two papers. In fact, some of the points they mentioned might be applied with advantage to Philadelphia. So that the smaller and far-off communities may not get all the credit, I want to call attention to the fact that both Dr. Mitchell and Dr. Pike spent most of their lives in large cities, and Dr. Jackson is a native Philadelphian; therefore, I think we can take credit for some of the work accomplished. It is amazing to contrast the former methods of treatment with those employed at the present time. The progress made has been remarkable, and it seems to me to be only logical for us to look forward to the time when the least important of the activities of the state hospital will be the care of the patient with mental disease. Rather will they be centers from which the doctrine regarding the prevention of mental diseases will be spread. I hope that Dr. Mitchell gets a larger per diem allowance for the care of his patients and also that he will use it for the care of patients with acute disease, for the study of mental diseases and for his extramural activities rather than for chronic cases. The allowance per diem is ridiculously low in this state, especially when we consider that in the Boston Psychiatric Hospital they rate the cost of the patients at $50 each a week. It seems a shame that we have to confess to being able to afford only $6.

When we see the outcome of this work in the future I think the first result will be a tremendous increase in the amount of mental disease, because, as more and better hospitals spring up, a greater amount of mental disease is uncovered; but, looking further than that into the far future, we can see actual decrease in the incidence of mental disease. Then the plans these men are formulating will bear their fruit.

Dr. John Wilson: I want to comment on the practical nature of the papers which have been presented to us. They have shown us in a most practical way how we as hospital workers can come in contact with the general public. Dr. Sandy brings up a practical thought: We cannot operate our state hospitals without money, and we cannot get the money from the people unless they know of our work. My wife recently attended a meeting in Harrisburg in regard to chiropractors. There are about 1,400 practicing in this state without licenses; in Montgomery County alone they have two legislators working for their interests, and they have produced a bill which is now being considered in Harrisburg. There were several hundred chiropractors in Harrisburg at the time the bill was introduced, while our medical societies were almost wholly unrepresented.

The point I wish to bring out is that apparently the chiropractors know the value of coming in contact with the people, and the state hospitals will

not secure sufficient appropriation for their needs unless we physicians get in touch with our legislators.

DR. DERCUM: I have long been interested in the extension of the functions of the hospitals for the insane, and I have witnessed their remarkable progress and their increasing influence in the community with great satisfaction. Listening to the papers this evening, I had great pleasure in learning what has been accomplished. It means that the hospitals for the insane are no longer separate institutions apart from the community, but that they are beginning to form an integral part of the communities in which they are located. Important results are being achieved, one of which has a most important bearing on the future, and that is the bringing about of an actual gain in the mental and physical health of the community as a whole. The day will doubtless come when the incubus of the insane, which now weighs so heavily on the state, will be greatly reduced. Syphilis and alcohol have played a large rôle in the past, and they are now being combated as never before. When given half a chance, Nature tends to right herself in spite of all the crimes that have been committed against her. The truth that stocks do right themselves — that they tend to swing back to normal — is evidenced by the fact that there are no family histories free from neuropathic or psychopathic factors. We need only to go back a sufficient number of generations to find them. And yet the prevailing stocks are healthy; in other words, the tendencies in biology are always toward normal, and interfering and complicating factors are, in the course of time, overcome. The rôle played by the hospital for the insane is certainly different at present from what it was thirty years ago, and this lends a much brighter outlook to the future.

DR. MITCHELL: One must approve most heartily of Dr. Strecker's suggestion that all necessary attention should be given to patients with acute conditions who may recover, that practice has been found helpful in restoring normal mental conditions, and that in every instance expense should not be considered when contrasting such patients with the chronic class for whom suitable provision can be made with much less financial expense.

Phychopathic hospitals can meet only a small percentage of the demand through the state for this service, but every hospital receiving patients can and should have psychopathic wards in which recoverable patients may receive every diagnostic and therapeutic aid available to neuropsychiatrists anywhere. No large state hospital is properly managed until medical and nursing services are developed to meet adequately the needs of incoming patients.

To bring about a reasonable development in our hospitals for mental diseases requires an enlightened public's demand for a betterment of conditions, that shall find expression in legislative action. Legislators are usually anxious to give the help to medical service that the public demands. Unfortunately, the public has been little interested in the treatment of patients with mental disease, and the driving force which will compel better arrangements for the care of patients with mental diseases in Pennsylvania must be developed. The most effective agency to accomplish this purpose is the educational result of a well organized effort for mental hygiene. The propaganda for improvement must be reasonable and rational. Extravagant claims, either for the necessity of better provisions or for the results that may be obtained, should not be presented. We should not claim that we can greatly reduce insanity in a given generation, or that we can effect miraculous cures by the adoption of new methods. There are few forms of mental trouble which we can materially

modify by any known method of treatment. We cannot replace the feeble intellect with normal mental capacity.

The work of prevention of insanity, the reduction of feeblemindedness and of the delinquent juveniles is one which will find its fullest expression in later generations, only after a more complete and careful medical and social treatment of juveniles have been followed for an indefinite period. But the preventive work which should be carried out more fully than ever before, in Pennsylvania or elsewhere, involves expense and effort on a scale with which our state is entirely unfamiliar. Here again we should be careful in our claims concerning results that are likely to follow.

Thousands of children and juveniles are allowed to develop antisocial conduct that could be corrected by a reasonable plan of prevention that should be expected in this state.

The establishment of clinics in connection with state hospitals is one of the best methods of striking effectively at the general causes productive of antisocial conduct; but here again, too much must not be predicted unless elaborate plans are made for careful and intensive work in individual cases.

The child clinic supervised by Dr. Truitt at Los Angeles had two full time physicians with eight full time social workers who, during the year of its operation, gave intensive study to only three hundred cases. This was, presumably, a model clinic, and the figures quoted give some indication of the expensive arrangements that must be made if best results are to be obtained in the study of any clinical group. It is improbable that comparable arrangements can be effected generally, and that hardly in our lifetime shall we see a general development of this work on the scale followed in the Los Angeles clinic. In the meantime we should utilize every agency available, both in the larger cities and in the country districts, for developing mental hygiene clinics. In the smaller towns and country districts mental hospitals must bear the burden of conducting the efforts that are being made to promote mental hygiene through clinical service. They cannot function properly in this state until they are more liberally supported by the legislature.

Book Reviews

THE MEASUREMENT OF EMOTIONAL REACTIONS. By DAVID WECHSLER, PH.D. Paper. Price $1.76. Pp. 181. Being No. 76, Archives of Psychology, New York City, 1925.

This monograph is devoted to "Researches on the Psychogalvanic Reflex," to the explanation and practical utilization of which the author has made substantial contributions. We may recall that Prideaux, in his painstaking review of the subject (Brain **43**:50-73, 1920), concluded that a good case had been made out "for further investigation into the psychological study of the psychogalvanic reflex. The observations so far recorded are small, and the opinions of the observers are often conflicting. But it would seem that we have in the psychogalvanic reflex a valuable objective sign, which may be able to help us in the elucidation of the many unsolved problems in psychological medicine, and which we cannot afford to disregard." Wechsler also points out how "incomplete and insufficient" is our "knowledge of the affective aspects of human experience" and how lacking are our available methods for "the measurement of the individual's emotional makeup." He reviews the numerous bodily manifestations which are called forth by affective reactions: variations of respiration, blood pressure and capillary pulse; diminished motor control (trembling, etc.); inhibition or excitement of gastric secretion or of intestinal peristalsis; alterations in the coagulability of the blood, in secretion of glands, in metabolism; changes in the character of the handwriting, the size of the pupil, the pressure of the cerebrospinal fluid, etc. None of these physiologic expressions of emotion has lent itself to "control and measurement — not even variations of blood pressure and capillary pulse" which seemed to offer the most promising opportunity. The psychogalvanic reflex, "while not free from sources of error particular to itself," has many advantages; it "is very easily evoked"; the magnitude of the response is easily controllable; the measuring instrument remains constant, or its variations may be calculated. The failure to obtain better results has been due in part to a lack of appreciation of "physical factors which may produce variations in the electrical conductivity of the skin" as well as of the "purely physiological reactions of the skin to the passage of an electric current." Another source of difficulty has been "the absence of a satisfactory method of measuring and recording the phenomenon." Before taking up psychologic correlations he therefore attempted to solve these difficulties.

The author devotes a chapter to a description of the galvanic response and two chapters to a discussion of the electrical behavior of the skin — and to the technic of the measurement of the galvanic response. Wechsler has devised a relatively simple apparatus (the photogalvanograph) which combines everything necessary for making an electrical measurement as well as the photographic record. The apparatus is portable, and a dark room is unnecessary. In the four chapters which follow there is a full discussion of physiologic mechanisms and psychologic correlations, thus clearing the way for the clinical applications.

"The psycho-physical analysis of the galvanic response . . . involves . . . the interrelation of three factors: (1) the initial (sensory) stimulus, (2) the intermediate affective state it evokes, (3) the physiological reaction."

While strong sensory stimuli may call forth strong reactions, "the galvanic response is never directly dependent" on these alone; but solely on their affective value for the individual. "The greater the emotion experienced, the greater, under the given conditions, will be the galvanic deflection." A correlation with association tests (using a special list of words) showed that the patients' subjective judgment of the affective value of the words did not always conform with the instrumental findings. This indicates in all probability "that the electrical changes were accompanied by affective reactions which were not conscious at the moment of their occurrence. In order to throw light on a "fundamental problem as regards the nature of emotivity, namely, whether, as in the case of general intelligence, there is such a thing as a factor of general emotivity," the author used a "battery" of varied stimuli in about thirty subjects. While his data are insufficient, they show a lack of correlation between the effects of stimuli involving orientation of attention and those of a purely sensory type, so that there is "some evidence that individuals probably tend to be specifically rather than generally emotional."

In the chapter on "Clinical and Practical Applications" the uses of the test as the "best simple indicator of affective tone" are detailed and the literature is brought up to date.

Dr. Wechsler's monograph is invaluable to those who are taking up this type of work, for he has solved many technical problems which have previously distracted experimenters from the essential clinical uses of the method. His work should result in a wide use of the instrument in the clinical laboratory, and, let us hope, will shed much new light on the nature of the emotions, particularly in the psychoses. This book is also of value to those who have a more general interest in the relation of bodily reactions to affective states, as the author has made a close analysis of the whole subject.

LES MANIFESTATIONS TARDIVES DE L'ENCÉPHALITE EPIDEMIQUE (FORMES PROLONGÉES ET REPRISES TARDIVES), PAR LE DOCTEUR GABRIELLE LÉVY. Preface du Professeur Pierre Marie. Avec 53 figures dans le texte. Paris: Gaston Doin, 1925. Price, 25 Francs.

Doubtless this is the most complete contribution on the subject which has appeared to date. As Pierre Marie says in the preface, although the epidemic of encephalitis has practically disappeared, we are constantly consulted by patients with the late manifestations. Consequently, this brochure is timely and of practical value. Dr. Lévy has devoted several years to this work, and has examined more than 200 patients, the basis of the present monograph being the personal study of 129 cases, all at the Salpêtrière.

The author discusses the difference between continuous and late or delayed (tardives) manifestations, the first being symptoms which persist from the acute stage, the second being symptoms which appear after a period of latency or after the patient apparently has made a complete recovery. Wisely, we think, the author declines to make a radical distinction. Our knowledge of the bacteriology and pathology of the disease is still too meager to permit us to draw the line between "chronic," "relapse" and "sequela."

For convenience, the author divides her cases into:

Parkinsonian syndrome, seventy cases; excito-motor syndrome, forty-three cases; eleven choreic; eighteen myoclonic; seven bradykinetic; seven facial movements; resembling torsion spasm, one case; respiratory form, ten cases; hemiplegia, one case; obesity, four cases. She hastens to add that such a

grouping cannot be hard and fast, as the same patient may change from one to another group, or present at the same time the symptoms of more than one type.

There follows a masterly description of the various forms of the excito-motor syndrome: choreiform, myoclonias and singultus, bradykinesias, tremors, facial and mandibular movements, psychomotor excitement, etc.

Sixty-one pages are devoted to the paralysis agitans syndrome of encephalitis in all its tragic details. We know of nothing in the literature so adequate.

In Chapter III (twenty-five pages) the author considers other motor disorders not easily classified: torsion spasm (a most remarkable and interesting manifestation), hypertonia without the parkinsonian syndrome, hemiplegia, paraplegia: sensory troubles and disorder of the special senses, including oculo-motor anomalies.

In Chapter IV are described a whole host of respiratory symptoms: the several types of insomnia, disturbances of temperature, circulation and nutrition (obesity).

After a brief discussion of the late mental symptoms of epidemic encephalitis, the author passes to a consideration of the prolonged or late symptoms of the disease in children, which are apt to be different from those observed in the adult.

Diagnosis and prognosis are succinctly presented.

Pathogenesis and pathology are covered in thirty-two pages, and adequately so, with excellent illustrations. The next fifty-six pages of close type are devoted to illustrative cases of the different types. A summary of eight pages and a bibliography (mostly French) of 796 references close the book. It is a work of the highest order, reflecting not only the industry and scientific attainments of the author, but also her good judgment and discernment of values. In fact, it is the most encouraging sign we have seen for a long time of the (perhaps) forthcoming woman regnant in medicine.

SERUM DIAGNOSIS OF SYPHILIS BY PRECIPITATION. By R. L. KAHN, Sc.D. Pp. 237. Baltimore: Williams & Wilkins Company, 1924.

During the past nineteen years numerous attempts have been made to evolve a precipitation test for syphilis as a substitute for the complement-fixation test. At the present time those of Sachs and Georgi, Meinicke, Vernes, Dreyer and Ward and Kahn are attracting most attention, particularly that of Kahn in this country.

In this monograph Kahn has briefly reviewed a portion of the very large amount of literature on the subject, and has described his own work with considerable detail, particularly the test which he has evolved for the serum diagnosis of syphilis. The literature bearing on comparative studies with his test and the Wassermann test is reviewed, with the general conclusion that the former possesses the sensitiveness and specificity of the latter while being technically simpler and more economical.

It is still too early, however, to pronounce definitely on the comparative merits of the two tests, as so much depends on the technic employed for conducting the complement-fixation test. The reviewer does not hesitate to state that his experience with the test as described in this excellent book has been satisfactory, not as a substitute for the complement-fixation test, but rather as a control to be conducted with each serum. Sometimes the precipitation test yields a truly positive reaction when the complement-fixation test is negative; the reverse occurs with equal frequency, although

in a general manner the Kahn test is likely to yield persistently positive reactions in treated cases of syphilis for longer periods of time than the complement-fixation test.

The precipitation test is technically simpler to set up than the complement-fixation test; but the preparation and titration of the antigen is no less laborious or complicated, the test requires almost as much time, and the readings are more difficult with weakly positive or doubtful reactions. After all, economy of time and materials are of much less importance than sensitiveness and specificity, and almost as much skill and experience are required for the proper conduct of the precipitation test as for the complement-fixation test for syphilis. Certainly the former cannot be readily made an "office test" as sometimes surmised, but undoubtedly Kahn has evolved one of the best methods known, which the reviewer predicts will be widely adopted as an excellent additional or control test for the serum diagnosis of syphilis.

CONTRIBUTION A L'ÉTUDE DES SYNDROMES DE LA RÉGION THALAMIQUE. By PIERRE HILLEMAND. Pp. 182. Paris: Jouve & Cie.

This is an excellent example of the best type of French thesis. Written by a well trained, capable and industrious worker under the guidance of a real master (Professeur agregé C. Foix), it is a complete but succinct statement of what is known of thalamic syndromes. Our knowledge of these symptom groups is due principally to study of cases of softening from vascular occlusion, these lesions being definitely limited and much less prone to cause confusing neighborhood symptoms than do tumors, hemorrhage and trauma.

Logically, the author begins by making a study of the blood supply of the thalamus; first by means of the literature (rather inadequate) and then by making injections into the cerebral arteries. From these investigations he concludes that the thalamus is supplied by five distinct arterial twigs — thalamoperforate, thalamogeniculate, premammillary, choroid and lenticulo-optic — and that to the occlusion of each of these irrigating mains belongs a different syndrome. Two of these symptom groups are well known: the classic thalamus syndrome of Déjerine due to occlusion of the thalamogeniculate twig, and one characterized principally by incoordination and intention tremor due to occlusion of the thalamoperforate artery. The many variations and combinations are well described, and an interpretation of the symptoms on an anatomic and physiologic basis is attempted. Then followed detailed reports, with microscopic examination (thirty-seven illustrations) of illustrative cases, and two and a half pages of conclusions which briefly sum up the entire situation in a masterly way.

THE PHYSIOLOGY OF MIND. AN INTERPRETATION BASED ON BIOLOGICAL, MORPHOLOGICAL, PHYSICAL AND CHEMICAL CONSIDERATIONS. By FRANCIS X. DERCUM, A.M., M.D., Ph.D., Member of the American Philosophical Society, Fellow of the College of Physicians of Philadelphia; Member of the Academy of Natural Sciences of Philadelphia; Professor of Nervous and Mental Diseases in the Jefferson Medical College. Second Edition, Reset. Philadelphia, W. B. Saunders Company, 1925.

The second edition of this work has filled a want in an interesting way. The author begins with a study of the motor functions of the ameba and its responses to its environment, and then traces some of the functions in unicellular and multicellular organisms and the gradual development of

affector and effector elements, their differentiation into nervous tissues, and the final accumulation of sensory and sensient cells with the development of consciousness, all envisaged from the physiologic point of view.

The author makes a naive apology to the religious-minded for his practical denial of the spiritual and soul features of the old psychologists. In nervous manifestations he adheres to the argument for synaptical contacts and withdrawals, and in this way explains various organic and inorganic nervous disorders. He believes in the electrical character of nerve transmission, and after developing the subject of the field of consciousness, the rôle of the thalamus, the synthesis of special sense impressions, speech, and the factors which influence the functions of the neuron, he gives a satisfactory review of the subject of instincts and tropisms, and then brings Einstein's theory into the interpretation of energy as concerning the nervous system.

In an addendum he takes up the question of the pathologic physiology of mind, discussing psychoneuroses, the essential deteriorations and dementias, and some of the effects of extraneous poisons.

In an appendix he pays his compliments to Freudism in a short, terse and snappy chapter, which terminates:

"Freudism stands on the same footing as Eddyism, Christian Science, and like forms of mental healing. Like the latter, it is mystic medicine."

While planned for lay reading, the book will be found of interest and distinctly instructive for those doing special work in neurology and psychiatry.

EINFÜHRUNG IN DAS STUDIUM DER NERVENKRANKHEITEN FÜR STUDIERENDE UND ÄRTZE. VON DR. ALFRED FUCHS, A. O. Professor für Psychiatrie und Nervenkrankheiten an der Universität Wien. Zweite, mbearbeitete und vermehrte Auflage. Pp. 491. Mit 117 Abbildungen im Text und 11 Tafeln in Lichtdruck. Leipsig und Wien: Franz Deuticke, 1925.

The first edition of this handy textbook appeared in 1911. As the title indicates, it is designed for students, and apparently is founded on courses of instruction in the examination of patients with disease or disorder of the nervous system. Much space is given to history taking, to details of examination and to the significance of signs and symptoms elicited.

This part of the book, though a bit pedantic, is excellent. It is a safe guide and full of information though the reading is not easy. Anyone who becomes familiar with these chapters will have a solid foundation on which to build a full knowledge of nervous diseases.

The part relating to the various diseases is much less satisfactory; sometimes too brief to be useful, not always up to date and not rarely inaccurate. The fact that eighteen pages are devoted to the pupil and ten to the tendon reflexes, with only five and a half pages on brain tumor, four on acute anterior poliomyelitis and five and a half on cerebral hemorrhage, thrombosis and embolism together, is rather indicative of the general character of the work. It is a good book for students but inadequate for practitioners.